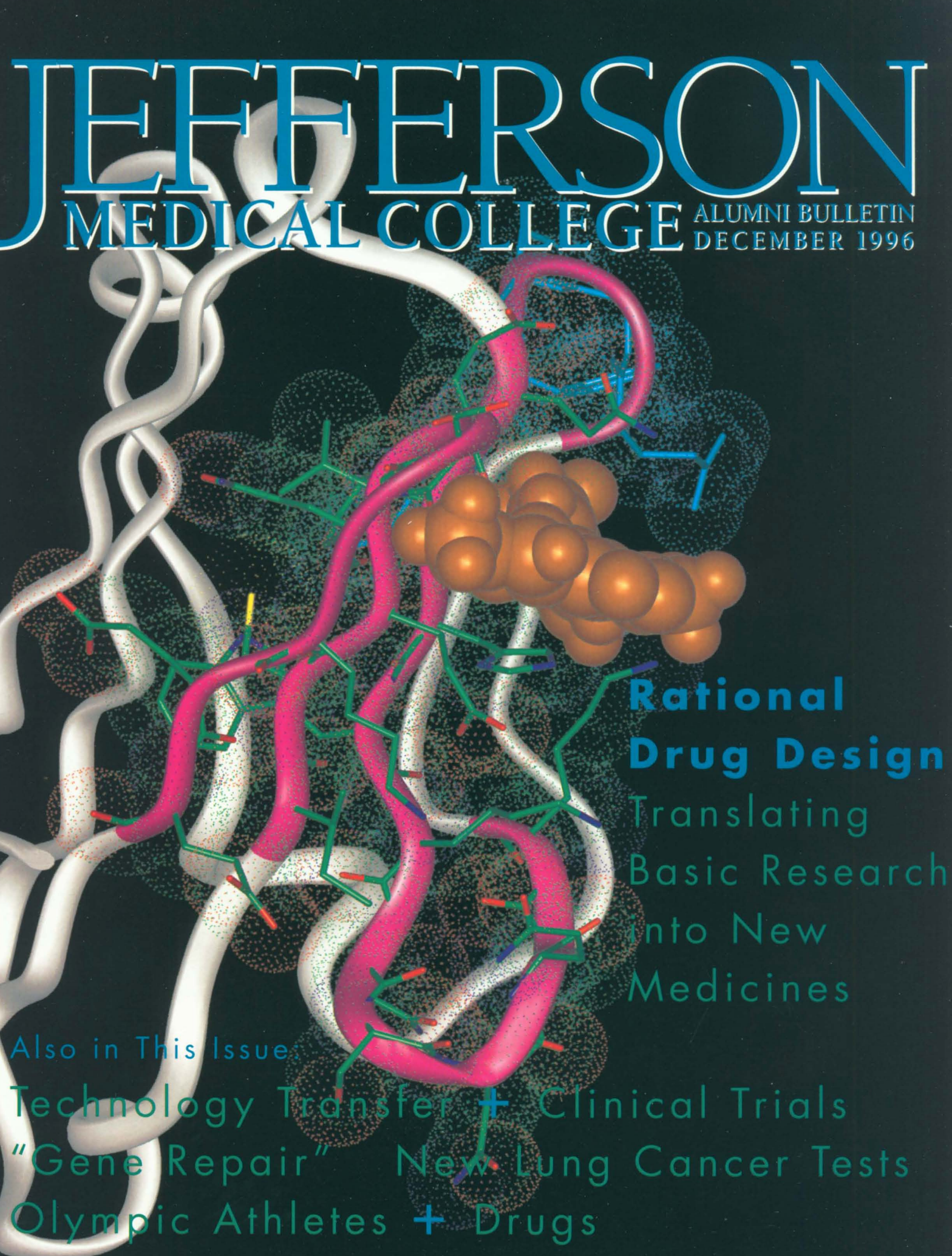
12-1996

Jefferson Alumni Bulletin – Volume XLVI, Number 1, December 1996

JEFFERSON MEDICAL COLLEGE

ALUMNI BULLETIN
DECEMBER 1996



Rational Drug Design

Translating Basic Research into New Medicines

Also in This Issue:

Technology Transfer + Clinical Trials

"Gene Repair" New Lung Cancer Tests

Olympic Athletes + Drugs

Upcoming Events

February 14, Friday
Alumni reception at the meeting of the American Academy of Orthopaedic Surgeons, San Francisco, CA

Receptions in California
February 18 Los Angeles
February 19 San Diego
February 20 San Francisco

February 22–28 Continuing Medical Education
Jefferson Anesthesia Conference for Cross Country and Downhill Skiers
Lone Mountain Ranch, Big Sky, Montana
For information call toll-free 1-888-JEFF-CME

March 1–2 Continuing Medical Education
Imaging of the Shoulder and Elbow with Emphasis on Medical Clinical Relevance
Jefferson Medical College, Philadelphia
For information call toll-free 1-888-JEFF-CME

March 5–8 Continuing Medical Education
24th Annual Course in Electrodiagnosis and Clinical Neurophysiology
Bluemle Life Sciences Building, Jefferson Medical College
For information call toll-free 1-888-JEFF-CME

March 14, Friday
Parents Day for the Sophomore Class and their families

March 23, Sunday
Alumni reception at the meeting of the American College of Physicians, Philadelphia, PA

March 23, Sunday
Alumni reception at the meeting of the American Academy of Dermatology, San Francisco, CA

March 31–April 4 Continuing Medical Education
Bermuda Shorts for Clinical Anesthesiologists
Sonesta Beach Resort, Bermuda
For information call toll-free 1-888-JEFF-CME

April 4, Friday Continuing Medical Education
Dermatology in General Medicine
Jefferson Medical College, Philadelphia, PA
For information call toll-free 1-888-JEFF-CME

April 13–14 Continuing Medical Education
Jefferson Foot and Ankle Advanced Imaging Symposium
Jefferson Medical College, Philadelphia
For information call toll-free 1-888-JEFF-CME

April 19–20 Continuing Medical Education
The Fourth Annual Cardiovascular Radiology Review Weekend
Jefferson Medical College, Philadelphia
For information call toll-free 1-888-JEFF-CME

April 24, Thursday
Alumni Annual Business Meeting

April 27, Sunday
Alumni reception at the meeting of the American College of Obstetricians and Gynecologists, Las Vegas, NV

May 9–10 Continuing Medical Education
Jefferson Cytopathology Review Course
Jefferson Medical College, Philadelphia
For information call toll-free 1-888-JEFF-CME

May 18, Sunday
Alumni reception at the meeting of the American Psychiatric Association, San Diego, CA

May 21, Wednesday
Reception and Dinner, Wilkes-Barre, PA

May 31, Saturday Continuing Medical Education
Cardiology: Balancing the Art and Science
Jefferson Medical College, Philadelphia
For information call toll-free 1-888-JEFF-CME

Reunion Weekend
June 6 Alumni Banquet
June 7 Clinic Presentations; Dean's Luncheon; Reunion Parties
June 8 Farewell Brunch

June 13–21 Continuing Medical Education
Barge Trip in Burgundy region of France—see page 11

June 22–27 Continuing Medical Education
Eastern Shore Medical Symposium, Rehoboth Beach, Delaware
For information call toll-free 1-888-JEFF-CME


Patrick J. Mattera

Jefferson Medical College Alumni Bulletin
Volume XLVI, Number 1
December 1996

Rational Drug Design
Translating Basic Research into New Medicines 4

Technology Transfer
Jefferson's Link Between Research and Industry 7

Clinical Trials
Jefferson's Link Between Research and Patient Care 9

World-Class Athletes and Drugs
Richard Cohen '65 Officiates at the Olympics 12

The Makings of the Compleat Physician 14

Major Alliance Links Jefferson with Mercy Health 17

"Gene Repair" Corrects Mutation Leading to Disease 19

Genetic Discoveries Lead to New Lung Cancer Tests 20

Alumni Can Participate in JeffHOPE 24

Student AMA Organizes Bone Marrow Drive 25

First Down in the Snow: JMC students are game, even after last year's blizzard. For more student activities, see pages 24-25.

The quarterly magazine
Published continuously since 1922

Address correspondence to
Attention: *Alumni Bulletin*
Jefferson Medical College
of Thomas Jefferson University
1020 Locust Street, Suite M-41
Philadelphia, PA 19107-6799

Alumni Bulletin Office: 215 955 7920
Fax: 215 923 9916
Internet: iedl72w@tjuvm.tju.edu

The Jefferson community and supporters are welcome to receive the *Bulletin;* please contact the address above.

Postmaster: send address changes to the address above. Second class postage paid at Philadelphia, PA
ISSN-0021-5821

This issue's cover features computer-generated images of a potential CD4-based drug developed at Jeff (see page 4). Rational drug design is providing the university with further opportunities in technology transfer (see page 7) and clinical trials (see page 9).

Medical Media Service

Ziwei Huang, Ph.D. directs a team of scientists who use state-of-the-art technology to design new drugs, like the one shown on the cover.

Rational Drug Design

Translating Basic Research into New Medicines

On the front and back covers of this issue, an organic inhibitor (the orange shape) designed by Dr. Ziwei Huang's laboratory at Jefferson is shown to bind to a surface pocket of the CD4 protein and thus block CD4-mediated T cell responses involved in transplant rejection and a number of autoimmune diseases. Using a computer, Dr. Huang and his colleagues have found this organic drug lead which is so successfully tailored to the nooks and crannies of the CD4 protein surface that it binds the CD4 target with high affinity and tremendous specificity.

The discovery of this and other potential new drug molecules using computer-based technology is being reported in the *Proceedings of the National Academy of Sciences USA* (January 7, 1997 issue) and is one of the latest examples of rational drug design at Jeff. "This is truly groundbreaking work," says Carlo M. Croce, M.D., Director of Jefferson's Kimmel Cancer Center and Kimmel Cancer Institute. "Many other proteins discovered here at the center can be looked at in this way to design new drugs for cancer and other human diseases."

In this article, we take a close look at the current status of Jefferson's rational drug design research, and the future promise it holds for realizing the university's vision in translating basic scientific discovery into new medicines for the coming century.

Rational drug design (also known as structure-based drug design) is an emerging approach that is revolutionizing the practice of drug discovery. Traditionally, a typical drug development process takes more than 10 years and costs about $100 million. Facing today's rapid changes in the health care environment, we can no longer afford such lengthy and expensive ways of finding therapeutic agents to combat human diseases. Rational drug design solves these problems through the use of innovative computer technology combined with many other disciplines to speed the development process.

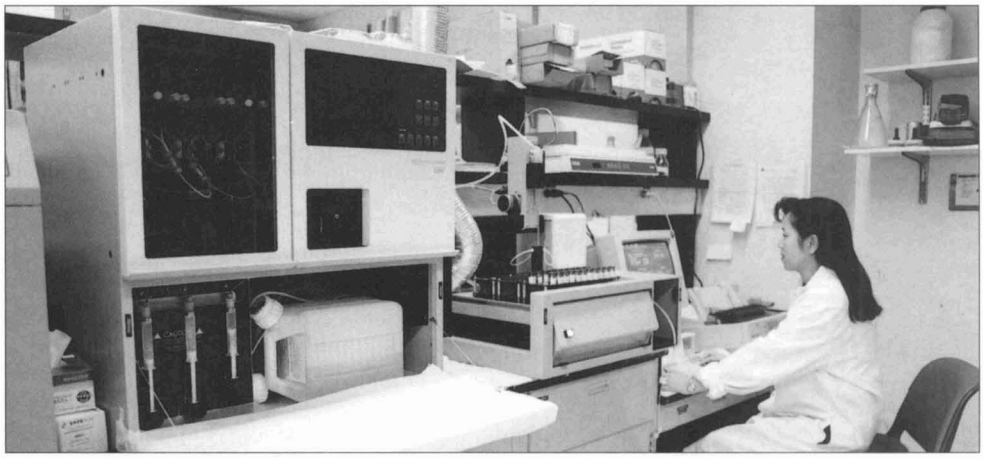
It begins with the identification of a molecular target such as a protein by genetic and molecular biological techniques, and the structural study of the target by high-resolution crystallography and NMR spectroscopy. The structural information about the target is exploited by the computer to design potential drug molecules that regulate the specific function of the target.

The designed molecules are then synthesized and modified using peptide and organic chemistry techniques, tested for biological efficacy in various in vitro and in vivo assay systems, and finally the most promising lead is generated for clinical trials in humans.

"Rational drug design has taken root at Jefferson and received a tremendous boost with the arrival of Dr. Ziwei Huang from the University of California, San Francisco, in early 1995," says Robert L. Comis, M.D., Clinical Director of the Kimmel Cancer Center. The Rational Drug Design Program was established with the vision of Dr. Carlo Croce and the strong support and resources provided by the medical college and the university.

The development of the Medical Science Division at the Kimmel Cancer Center, under the direction of Dr. Comis, has provided the environment critical for this type of research.

The projects' recent success is due to many factors, explains Dr. Huang. The geneticists and molecular biologists at the Kimmel Cancer Institute have discovered many genes and their protein products implicated in various pathological conditions, thus providing a bewildering array of potential targets for drug design studies. The establishment of the X-ray crystallographic and high-field NMR spectroscopic facilities at the institute has provided important tools to obtain structural information necessary for initiating the design of a drug. Finally, the computer modeling and peptide synthesis facilities have been essential.



After being designed on the computer, molecules are synthesized and modified at the Peptide Synthesis Facility, located in the Bluemle Life Sciences Building and directed by Dr. Huang. These potential peptide-based drugs are then put into preclinical studies.

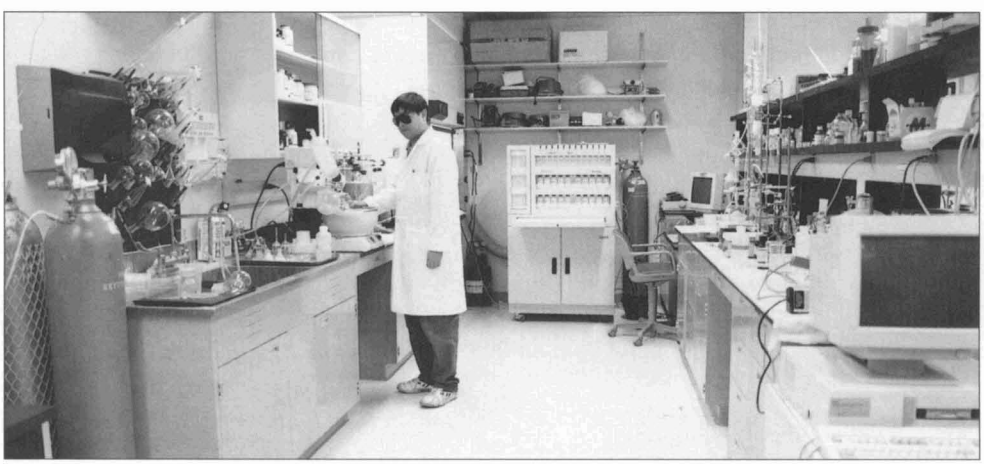
Currently Dr. Huang's lab has a network of state-of-the-art computers including a four-processor mini-supercomputer. The Peptide Synthesis Facility directed by Dr. Huang is equipped with four fully automated synthesizers that can produce high-quality, biologically active peptides as potential drugs for both small-scale, in vitro assays and large-scale, preclinical animal studies. These research infrastructures, together with other activities and programs in technology transfer and clinical trials (see the following two articles, pages seven and nine), are integral to Jefferson's mission to combine strong basic research with clinical excellence to develop a new generation of human therapies.

The recent development of CD4-based drugs by Dr. Huang's team serves to highlight the general strategy of rational drug design. CD4 is a glycoprotein expressed on the surface of a T cell. CD4 contacts another antigen-presenting protein called major histocompatibility complex (MHC) class II during the early stage of the T cell response to an antigen. Because of this, CD4 plays a critical role in regulating the immune system which, if it goes awry, could lead to pathological consequences, such as organ transplant rejection and autoimmune diseases.

To control the undesired immune response in these diseases, therapeutic strategies such as an anti-CD4 antibody have been developed. However, the clinical value of these antibody-based therapies is limited due to their immunogenicity when used in humans. To overcome this problem, Dr. Huang's group resorted to a rational drug design approach to generate novel, small molecular CD4 inhibitors. In contrast to an antibody, small molecules (such as peptides or organic compounds) are not immunogenic and therefore can be used for long periods of time.

Using computers, Dr. Huang's team looked at the three-dimensional shape of the CD4 protein and designed small peptides that could block CD4-mediated immune function. These computer design and peptide synthesis studies have led to the discovery of a small cyclic heptapeptide which has been shown by the collaborating immunology laboratory of Dr. Robert Korngold at Jefferson to be highly effective in animal models for human multiple sclerosis, organ transplant rejection, and graft versus host disease (GVHD) following bone marrow transplantation.

In addition to the design of peptide drugs, the computer is also used to select potential organic CD4 inhibitors from large pools of existing compounds. Using



The Organic Synthesis Facility, recently established within Dr. Huang's laboratory, provides an essential tool for producing a future generation of organic drugs. According to Dr. Huang, the initial peptide drugs will eventually be replaced by more cost-effective and orally available organic molecules.

sophisticated modeling and graphics software, Dr. Huang and his colleagues have identified promising organic inhibitors of CD4 function. Compared to the CD4 peptide drug, these second-generation organic drugs possess several advantages: their non-peptidic structures are less susceptible to enzymatic degradation and thus are more stable; they could be taken through the oral route which is most desirable in terms of patience compliance; and they are easily synthesized using inexpensive materials, which significantly lowers the cost of the therapeutic treatment.

The computer screening approach, as demonstrated in the discovery of organic CD4 inhibitors, is a powerful tool in the search for perfect drugs. In the past, many drugs were found from a traditional process of random screening of 100,000 to 500,000 compounds. In contrast to this laborious and expensive random testing, the computer-based strategy as used in the CD4 study took less than a month to complete the screening of approximately 150,000 compounds, and cost very little since the testing was done on the computer instead of test tubes and animals. "The organic drugs designed by the computer should be far better than the antibodies, and these studies will open new avenues for the development of effective medicines," says Hilary Koprowski, M.D., Director of Jefferson's Center for Neurovirology.

"Rational drug design is a team effort, and the CD4 project is a good example," points out Dr. Huang. The CD4 peptide and organic inhibitor studies have involved the ***computer modelers*** and ***chemists*** of Dr. Huang's lab including Song Li, Takashi Satoh, Jimin Gao, Xiaobing Han, Daniel Butcher, Zhaowen Luo, Simei Shan, Zhixian Lu, and Zhengdong Wu; the ***immunologists*** of Dr. Korngold's lab including Thea M. Friedman, Andrea E. Edling, Ute Koch, Swati Choksi, Robert Townsend, Joseph C. Marini, Ryszard Wiaderkiewicz, and Anna Wiaderkiewicz; and the ***NMR spectroscopists*** of Dr. Markus W. Germann's lab including James M. Aramini. According to Dr. Huang, this multidisciplinary collaboration and close teamwork have been essential to the progress made in the CD4 project.

Clinical Trials Will Begin Soon

Through close collaboration, Dr. Huang, Dr. Korngold, and clinical colleagues from the Translational Research and Bone Marrow Transplant Programs at the Kimmel Cancer Center have progressed to the point where a clinical trial is imminent. The remarkable aspect of the peptides is that there is no toxicity associated with their use in animals. Plus there is clear-cut synergy with existing medicines used for GVHD in humans such as cyclosporin. GVHD is the principal risk factor affecting the survival of cancer patients undergoing bone marrow transplantation.

During 1997 the researchers will evaluate both the side effects and activity of the CD4 peptide in patients who are at high risk for severe GVHD after bone marrow transplantation. These studies will be under the direction of Neal Flomenberg '76, Director of the Bone Marrow Transplant Program. Other clinical studies of the peptide will be conducted in patients with multiple sclerosis.

In addition to their intrinsic importance, these initial trials will lay the groundwork for employing the new organic molecules discovered from the computer screening. "We are very excited about the clinical potential of these novel CD4 drugs," says Dr. Comis. "They will point out the future direction of our translational research."

The CD4-based drugs, if they successfully pass human clinical trials and reach the market, will find many clinical applications for autoimmune diseases such as multiple sclerosis and rheumatoid arthritis and bone marrow and organ transplantation. Their commercial potential will be enormous as there is an estimated billion-dollar market for such drugs.

For this reason, Jefferson's drug design programs have attracted the attention of a number of pharmaceutical companies and investment groups which have already expressed strong interest in working with Jefferson to commercialize these drugs. "The drug design research carried out at Dr. Huang's laboratory represents the type of broadly applicable platform technology that is particularly well suited for collaboration with industry," notes Jussi J. Saukkonen, M.D., Dean of the College of Graduate Studies and Vice President for Science Policy, Technology Development, and International Affairs. "The involvement of the pharmaceutical industry will not only facilitate the development of commercial products, but also provide important financial support to further expand the basic research at Jefferson."

"This is another case substantiating the fact that progress in science is not made without risk," observes Joseph S. Gonnella, M.D., Dean of Jefferson Medical College and Senior Vice President for Academic Affairs at Thomas Jefferson University. "The university has made a huge investment in translational research of which this effort is a major part. And it is paying off. This approach will not only save prolonged trial and error and bring benefits to the patient that much sooner, it can also be expected to bring rewards to the university in increased clinical trials and stronger relationships with industry."

In just two years Jefferson's Drug Design Program has generated a peptide drug for human clinical trials and several organic molecules in the pipeline to be developed into second generation of cost-effective, orally administered drugs.

Most importantly, the technology developed from these studies will have general application for developing new medicines for other human diseases. Rational drug design will play a prominent role in Jefferson's mission to link basic research and patient care. "Jefferson is fortunate to have such a dedicated and talented drug design team," says Paul C. Brucker, M.D., University President. "I look forward to the future development of these translational research efforts."

Feature by Malcolm Clendenin

Technology Transfer

Jefferson's Link Between Research + Industry

John J. Gartland S'44

Since its founding, Jefferson Medical College has earned a reputation for clinical excellence and for producing good doctors. Prior to 1980, except for a few bright spots like the Cardeza Foundation, sponsored research had not been a prominent activity at Jefferson. During the early 1980s, the Board of Trustees of Thomas Jefferson University recommended that the base for Jefferson's excellence be broadened by increasing the research effort. The Strategic Plan adopted by the Board of Trustees in 1982 recommended a concerted effort be made to broaden the research mission at Jefferson, and additional capital for the needed faculty and for the needed facilities was approved. This recommendation and the additional financial support presented Dean Joseph S. Gonnella, M.D. with a mandate to recruit more research-oriented faculty while, at the same time, to maintain Jefferson's reputation for clinical excellence. In short order, Drs. Emanuel Rubin, Darwin Prockop, Jouni Uitto, and Willis Maddrey, among others, joined the Jefferson faculty and formed a research focus which, in turn, attracted more research people and more research dollars.

There is general agreement among medical research institutions that success in an institution's research mission is measured best by its share of research dollars obtained through competitive awards from the National Institutes of Health (NIH). In 1985 Jefferson obtained five million dollars in NIH funding and ranked 78th in research funding awards among U.S. medical schools. By 1995, Jefferson had increased its amount of NIH funding to 46 million dollars and its research ranking among U.S. medical schools had risen to the 36th position. The success of Jefferson's research effort can be understood by considering the *rate of increase of its share* of total funding by the NIH. Jefferson is second among all U.S. medical schools in the rate at which its portion of total U.S. research funding has grown over the period 1985–95.

The results of good medically oriented research is scientific achievement which can result in discoveries to improve patient care, or in technologies and products with marketable possibilities. The link between research and patient care at Jefferson is the Office of Clinical Trials (see pages 9–10). The link between research and industry at Jefferson is the Office of Technology Transfer which deals with patents and licenses of new discoveries or inventions of faculty or staff. Jefferson's link to industry began to be forged on an ad hoc basis in 1980. The first university patent policy was formulated in 1982, and establishment of the Office of Technology Transfer followed in 1984.

The commercial aspect of a Jefferson discovery or invention is handled by the Office of Technology Transfer. This program was created at Jefferson to capture the opportunities in basic and clinical research and to develop them into marketable products in a timely manner. The development of medical technology is a lengthy process, extending from the basic discovery through the development of products. This is followed by laboratory testing, clinical trials, regulatory approvals, and finally commercial introduction. Taking a technology or product from a basic idea to an actual product that can benefit the whole population is a task which may be accomplished best by combining the research and clinical capabilities of a university like Jefferson with the product development, manufacturing, and marketing capabilities of industry. The technology transfer program at Jefferson seeks to facilitate this development by securing patent protection to give industry the incentive to invest significant resources in development. This is followed by either licensing the technology or product to an existing company, or to a new company formed specifically to develop the new Jefferson technology or product.

Abram M. Goldfinger, Director, Office of Technology Transfer, has an electrical engineering degree from M.I.T., an M.B.A. degree from the Wharton School of the University of Pennsylvania, and an industry background in research and development. He began at Jefferson in 1987 as a business venture analyst in the Office of Technology Transfer and was made Director in 1991. He likes what he does at Jefferson because it combines science and technology with business, which is a good fit with his educational background. He says that working with Jefferson researchers to see businesses created and products developed based on that research is rewarding. Assistant Director Richard W. Miller has a bachelor's degree in biology and a Master's degree in management and experience in the biotechnology and pharmaceutical industry. Administratively, the Office of Technology Transfer reports to Jussi J. Saukkonen, M.D. who, in addition to being Dean, College of Graduate Studies, is Vice President for Science Policy, Technology Development, and International Affairs. Dr. Saukkonen has sign-off authority on all commercialization agreements negotiated by the Office of Technology Transfer. In addition, Gerald Litwack, Ph.D., Associate Dean for Scientific Affairs,

must approve agreements involving research at Jefferson. All legal agreements put together by the Office of Technology Transfer are reviewed by University Counsel before being signed.

In addition, the technology transfer effort at Jefferson receives oversight both from the university and the Board of Trustees. The Biotechnology Committee of the Board of Trustees was formed specifically to oversee the University's efforts and activities in this area. This committee determines how aggressive a posture Jefferson should take in this area, offers advice and sets policy on such activities as the formation of new companies and the taking of equity in new companies. The Technology Transfer Advisory Committee, a university management committee, is mainly advisory in function to ensure that Jefferson's technology transfer efforts are conducive to the general welfare of the university and are consistent with other university objectives.

Jefferson's current patent policy stipulates that the university owns the rights to any invention made or developed with university funds, equipment, facilities, or personnel. University owned technology may be patented and licensed either exclusively or non-exclusively. The inventors receive a share of the income derived from such licenses, and the remainder is applied to research and educational purposes at the University. Copyrightable works created for university purposes in the course of the creator's employment also are owned by the university and licensed through the Office of Technology Transfer.

The University Patent Committee plays a role in the interpretation and implementation of the patent policy. Chaired by Dr. Jussi J. Saukkonen in his capacity as Vice President for Science Policy and Technology Development, the Committee membership represent the faculty and the administration and are appointed by the University President.

Abram Goldfinger explains how the technology transfer process works at Jefferson. A Jefferson researcher notifies the Office of Technology Transfer of the development of a new technology or product which the researcher believes has commercial possibilities. The first step for the Office of Technology Transfer is to do a market analysis and review the patentability of the technology or product. If these reviews are favorable, Mr. Goldfinger files for a patent. While it takes about three years to obtain a patent, Goldfinger points out that the act of filing for a patent establishes a proprietary position for Jefferson which can be licensed. Next, the Office of Technology Transfer identifies companies with the appropriate resources to collaborate with Jefferson in the development and marketing of the technology or product. Picking a company as a partner in the venture may hinge on whether the company demands an exclusive contract or will accept a non-exclusive contract with Jefferson. If an existing company is selected to develop the technology or product, Jefferson gets licensing fees and royalties and, possibly, research funds. Jefferson may decide that the best way to develop the technology or product is to seek the formation of a new company. In that event, the Office of Technology Transfer develops an outline of a business plan and approaches venture capital firms or other investment groups to form the company. Jefferson generally does not invest funds in these ventures but, once a new company is formed, Jefferson receives equity in the company and, frequently, additional research funding.

Abram Goldfinger cites two recent examples of taking a Jefferson discovery to market. A vector system for gene therapy was developed at Jefferson which is capable of correcting errors in the DNA sequence, thus it may be broadly useful for gene therapy as well as in other applications. A patent application was granted in 1996. License and research agreements were signed in 1994 with Kimeragen, Inc., Newtown, PA, a new company formed to commercialize this technology. The agreement with the university includes Jefferson receiving equity in Kimeragen, Inc.

The second example involves a cancer vaccine which was developed at Jefferson for treating melanoma and other forms of cancer. The vaccine uses a patient's own tumor cells which are irradiated and modified to stimulate an immune response against other tumor cells. Clinical trials have been conducted in over 200 melanoma patients at Jefferson. After surgical removal of the tumor, the vaccine treatment increased the percentage of patients remaining disease-free for four years from 20 percent to 60 percent. A patent on the technology was issued in 1994. License and research agreements were signed in 1995 with Avax Technologies, Inc. of Kansas City, Missouri, a new company formed to commercialize this technology. Jefferson receives equity in this company.

Technologies developed at Jefferson during 1995–96 spanned a broad range of biomedical disciplines. ***Pharmaceuticals*** were developed which may prevent or treat major diseases, including multiple sclerosis, rheumatoid arthritis, fibrosis, heart disease, cancer, AIDS, stroke and malaria. ***Medical devices*** were developed for a variety of applications, including catheters for diagnosing and treating heart disease, systems for improving the quality of x-ray machines and other imaging equipment, improved surgical instruments as well as systems to help restore proper functioning of the heart and blood vessels, provide speech and mobility, and repair skin and cartilage. ***Diagnostics*** were developed to provide earlier detection of some diseases. Jefferson researchers have developed more sensitive methods to determine the presence or extent of prostate, colorectal, and cervical cancer, smooth muscle tumors, AIDS, orthopaedic infections, and hepatitis B, as well as to localize internal infectious foci. Tumor suppressor genes which play a role in a number of the most frequent types of cancer were identified, and which may allow the development of new treatments for cancer. Finally, ***reagents*** were developed to store and cultivate cells, including blood components for

continued on page 10

Clinical Trials

Jefferson's Link Between Research + Patient Care

John J. Gartland S'44

The initiative started during the 1980s to strengthen and increase the research effort at Jefferson has resulted in an investment in outstanding scientific talent and modern research facilities that has enabled Jefferson to be recognized now as a leading medical research center. This research initiative also has resulted in the development of an infrastructure at Jefferson where teams of recruited basic scientists with outstanding reputations complement Jefferson's acclaimed clinicians. The resulting collaboration between basic scientists and clinicians enables Jefferson to take research breakthroughs from the laboratory and quickly translate them into patient care benefits. In this day and age, innovative clinical research performed at academic medical centers must involve collaboration between basic scientists and clinicians.

One part of the comprehensive plan envisioned by Dean Joseph S. Gonnella, M.D. to ensure Jefferson's future as a leading academic medical research center is to take advantage of this new collaborative relationship by increasing the amount of clinical trials activity carried out at Jefferson. The administrative and scientific leadership at Jefferson is committed to the expansion of clinical trials because they represent the link between research and patient care at Jefferson. Associated with this initiative is the fostering of innovative relationships with private sector organizations for the exploration and evaluation of new compounds and devices to improve patient care. ***The strength of these new innovative relationships is built on Jefferson's ability to access the large patient populations necessary to conduct Phase III clinical trials through its partnerships such as the Jefferson Cancer Network, the Jefferson Health System, and the Medical Center of Delaware, among others.***

The first step in making a strengthened clinical trials activity a reality at Jefferson was to build the campus infrastructure. Dean Gonnella chose Gerald Litwack, Ph.D. as the architect for this effort. Dr. Litwack, a noted researcher in his own right, was Chairman of the Department of Pharmacology at the time of his selection. He is now Chairman of the newly combined Department of Biochemistry and Molecular Pharmacology and Associate Dean for Scientific Affairs. Dr. Litwack began by restructuring the former Office of Research Administration into a new entity, the Office of Scientific Affairs whose major areas of responsibility are 1) research administration, 2) clinical trials, 3) corporate/industrial relations, 4) misconduct in research, 5) research safety, and 6) government liaison.

Research activity arising out of a scientific discovery, such as a clinical trial, is administered by the Office of Scientific Affairs. The division of Research Administration in the Office of Scientific Affairs signs off on all clinical trials contracts. The Institutional Review Board (IRB) also comes under the Research Administration division of the Office of Scientific Affairs. The IRB is charged with the federally mandated responsibility for review of all protocols involving human subjects. The Office of Scientific Affairs works closely with the Office of Technology Transfer and with the Office of University Counsel in arranging industrial contracts and agreements. Administratively, the Office of Scientific Affairs is part of the medical college and reports to Dean Gonnella.

Because clinical trials were planned to be a major focus of the Office of Scientific Affairs, Dr. Litwack selected John J. Schrogie, M.D., a clinical pharmacologist and founder and CEO of the Philadelphia Association for Clinical Trials (PACT), to direct the clinical trials office within the Office of Scientific Affairs. This office deals directly with pharmaceutical companies, answers their questions, addresses their concerns, and becomes their facilitator in instituting clinical trials at Jefferson. Drs. Litwack and Schrogie, together with Thomas Murray of the Clinical Trials Division, developed an attractive handbook which highlights Jefferson's centers of excellence and clinical faculty, their research interests, and their past experience or potential experience in testing new drugs or devices with patients in clinical settings. This handbook, which explains the depth and breadth of Jefferson's expertise and capabilities in conducting clinical trials, was mailed to 250 pharmaceutical companies and contract research organizations to encourage them to match their needs with Jefferson's capable clinicians and basic scientists. In addition, visits were made to academic institutions with experience and success in conducting clinical trials in order to learn from their mistakes and from their successes. As Dr. Litwack explains, these efforts are a matter of educating these companies about Jefferson's capabilities in providing a site for their clinical trials, and then being able to deliver seamless service at competitive rates.

Additional space for research facilities was secured by the recent Jefferson purchase of the former Western Union Building at 11th and Locust Streets. Another piece of the clinical research infrastructure on campus is the new Clinical Research Center on the 11th floor of the Thompson Building. The center, under the current direction of Scott A. Waldman,

M.D., Ph.D. (see page 21), is an organizational component of the Department of Medicine and possesses the facilities and staff to provide the inpatient and outpatient resources needed to accomplish clinical trials. Representatives from companies interested in pursuing clinical trials which would be appropriate for the Clinical Research Center are given tours of the facility. If appropriate, they are then put in touch with interested faculty members to develop a suitable protocol for the proposed clinical trial.

The clinical trials division at Jefferson has been organized to provide research sponsors with a single office for assistance in identifying investigators whose clinical trial interests, experience, and patients match the study requirements of their protocols. As Dr. Litwack points out, clinical trials now are becoming a big business in this country. It is difficult for most medical universities to be competitive in attracting clinical trials because of their associated overhead. The effort put forth to date by Jefferson to become more involved with clinical trials has helped them become more competitive in this marketplace. Most of the effort to date has been directed to contract research organizations and pharmaceutical companies. A contract research organization is a private or public clinical research organization that acts as a middle man, a broker, or a clearing house in clinical trial activities. They are used mainly by pharmaceutical companies to arrange for clinical trials because they usually have good scientific contacts, and can set up single-center or multicenter trials. They also monitor the progress and conduct of the clinical trial. Negotiating with a single clinical trials office, such as the one at Jefferson, is an attractive incentive for contract research organizations and pharmaceutical companies, particularly after their representatives have been given a tour of Jefferson's facilities and sensed Jefferson's capabilities.

Dr. Litwack explains how the clinical trial process works at Jefferson. A proposal for a clinical trial is received by the clinical trials office. The proposal details what the sponsoring organization wants to accomplish and specifies the number and type of patients needed for the trial. The office of clinical trials identifies faculty clinical researchers whose interests correspond with the needs of the proposed trial and who may be willing to participate. During the negotiation process, one particular faculty researcher is identified by the involved department, or the department chairman, as the Principal Investigator (P.I.). The P.I. develops a budget for the proposed clinical trial and submits it to the proposing contract research organization or pharmaceutical company. This budget also includes all direct costs incurred by the Investigative Drug Service, a function of the Pharmacy and a service that is useful in many Phase I and Phase II clinical trials. Jefferson charges 25 percent of the direct cost of the clinical trial as its indirect cost. If the submitted budget is accepted by the sponsoring organization, the involved individuals set up their own process and initiate the clinical trial after receiving approval from the Institutional Review Board. After the clinical trial begins, the clinical trials office has only a helping and advisory function. The clinical trial investigators have the responsibilities of understanding the treatment protocol of the clinical trial, of following the clinical trial guidelines faithfully, and of reporting the results of the clinical trial scrupulously.

Dr. Litwack believes the clinical trials initiative is going well at Jefferson. He says the office of clinical trials often receives two to three new proposals per week. He explains that Phase I clinical trials test the effects of new products on normal people to look for possible toxic reactions, while Phase II and Phase III clinical trials test the effects of new products on a class of patients with a specific disease or disorder. Budgets for Phase II and Phase III clinical trials usually provide a source of funding for the involved clinical researchers. While the details of specific clinical trials are confidential until the trial is completed, Dr. Litwack says that the clinical trials now ongoing at Jefferson involve a wide variety of large and small pharmaceutical companies, and include such diseases and disorders as stroke, AIDS, cancer, including breast cancer, gastrointestinal disorders and rheumatoid arthritis. He points to a pile of between 10 and 15 new clinical trial applications awaiting presentation at the next meeting of the Institutional Review Board.

The mandate given to Dean Gonnella in 1982 to increase Jefferson's prominence in research and his comprehensive plan to fulfill that mandate appear to have been successful. The fruits of this effort have spread Jefferson's reputation worldwide, have brought additional patients to Jefferson, and have been a source of additional funding. During fiscal year 1996, in addition to NIH research awards, Jefferson received 22.5 million dollars from corporate research funding and clinical trials revenue. The alumni can be assured that Jefferson's future as a leading academic medical center and as a medical college that graduates good doctors with excellent clinical skills now is brighter because of the organized and effective way this research initiative is being implemented.

Technology Transfer, from page 8

transplantation. A variety of cells which are useful for research purposes also were developed.

Over the past two and one-half years, 10 new companies were created based on technologies developed at Jefferson; these are companies in which the university has or will receive equity. Twenty U.S. patents were issued to the university during fiscal year 1996, a 67 percent increase over fiscal year 1995. In 1995, Jefferson ranked 29th of all U.S. universities in patents issued. During fiscal year 1995–96 corporate support for university research amounted to 11.4 million dollars, in addition to 1.75 million dollars received from licensing revenues. Viewed from the perspective of 15 years, Jefferson's decision to add a research component to its acclaimed reputation for clinical excellence can be judged to have been a wise one.

Jefferson Medical College Alumni Association invites you to join a

Barge Trip in Burgundy

June 13–21, 1997

An educational getaway: enjoy the beauty of the Burgundy region of France by hotel barge with fellow Jeffersonians. Hosted by William V. Harrer '62, past Alumni President and Professor of Pathology. General medical update topics will be presented by faculty and alumni, led by Jerome J. Vernick '62, past Alumni President, Clinical Professor and Director of the Trauma Division

Friday, 6/13 ***Arrive in Paris*** This evening, professional wine and food authority Melba Mauviel will host a "Harmony in Food and Wine" dinner at a charming Parisian restaurant. This unique and delightful "expérience gastronomique" will prepare us for our cruise through one of France's most famous wine regions. Melba will join us later in Burgundy to accompany us to some of her favorite vineyards: Pommard, Meursault, Nuits St. Georges.

Saturday, 6/14 ***Travel in First Class on the TGV express train to Dijon, disembarking for lunch*** Continue by motor coach to our barge. Our afternoon cruise to Longecourt-en-Plaine begins with a champagne welcome.

Sunday, 6/15 ***Morning Cruise to Lovely St. Jean-de-Losne*** After the morning cruise to St. Jean-de-Losne we will drive to nearby Dole for a walking tour.

Monday, 6/16 ***Tour of Beaune*** The river Saône brings us to Verdun-sur-le-Doubs, where we board a motorcoach for world-famous Beaune, capital of Burgundy's wine region. After a tour of Beaune and its 15th-century hospices, we return to the barge.

Tuesday, 6/17 ***Cruise to Chalon-sur-Saône*** After a morning cruise to Chalon-sur-Saône, we embark on a shore excursion to Dijon. A tour shows us the historic city center, with time to browse in Burgundy's largest open market. Return to the barge for lunch and an afternoon cruise to Chagny.

Wednesday, 6/18 ***Arriving at Chagny*** The heart of the Burgundian vineyards, today's excursion shows us the area where 12th-century monks first set up their presses. We also visit a wine wholesaler to taste some local vintages on tap.

Thursday, 6/19 ***St. Léger-sur-Dheune (Cruising)*** We visit the fortress of Rully, private castle of the Comte d'Aviau de Ternay. Back at the barge, we gather for a farewell dinner tonight, our last on board.

Friday, 6/20 ***TGV express back to Paris*** We connect with TGV express back to Paris, arriving early afternoon. Overnight in Paris.

Saturday, 6/21 ***Back to U.S.*** An extra day in Paris can be arranged for those wishing to extend their French experience.

Rates

The rate of $3400/person includes: in Paris, two nights lodging with buffet breakfasts and special wine tasting/dinner, hotel transfer to train station, round-trip first-class TGV, Paris-Dijon, all transfers to and from barge, accommodations, breakfast, three-course buffet lunches, four- to five-course dinners, all bar drinks and unlimited wine with meals, morning coffee, afternoon tea, all excursions and entry fees, use of bicycles while barging, all taxes. The tour is organized and escorted by Adri Peacock, Ph.D. in Romance Languages and French, travel specialist since 1981.

Air transportation between U.S. and Paris is NOT included. Round-trip airfare from Philadelphia departing June 12, 1997 will be approximately $585.00. Comprehensive travel insurance is recommended.

1) Reserve Now for the Trip

Contact: Adri Peacock, Travel Specialist
Routes de France Travel, Inc.
4839 Olmos Street, El Paso, TX 79922
915-581-6913 or FAX 915-587-5725

Reserve NOW. Space is limited. Deposit of $500 per person insures your place on the barge. Balance of $2900 due March 13, 1997.

2) Register Now

To register, mail the form below to: JMC Office of CME, Alumni Trip, 1020 Locust Street M-32, Philadelphia, PA 19107. ***Enclose your registration fee of $250.00 payable to JMC Office of CME.*** For questions regarding Continuing Medical Education credits, call the JMC Office of CME at 215-955-6992 or 1-888-JEFF-CME or fax 215-923-3212.

Name _____ Class Year or Jeff Affiliation _____

Guest Name _____

Preferred Address _____

_____

City _____ State _____ Zip _____

Daytime Phone _____

❑ Yes, I am willing to give a one-hour educational presentation.

Thomas Jefferson University | Jefferson Medical College

World-Class Athletes & DRUGS

Richard Cohen '65 Officiates at the Olympics

John J. Gartland S'44

Jefferson was represented ably during the 1996 Summer Olympic Games in Atlanta by Richard W. Cohen '65 who served as Chairman of the Doping Control Program for this Centennial Olympiad. The interesting story of how he achieved this responsible position for the 1996 Summer Olympic Games was shared with the *Bulletin*.

After Jefferson graduation, he completed an orthopaedic surgery residency at the University of Pennsylvania, was board-certified, and in 1970 began an orthopaedic and sports medicine practice in Norristown, PA. Spurred by an interest in organizational medicine and an interest in civic activities shared with his wife, Dianne, they began to consider the possibility of relocating to another area holding more promise of growth and offering more opportunities for fulfilling their other interests. After a period of deliberate study, they selected Atlanta, GA as their new home and moved in 1972. Dr. Cohen joined a friend from Philadelphia in practice in suburban Atlanta and the Cohen family remains convinced that their choice of new home and practice setting was the correct one for them.

As Dr. Cohen's orthopaedic practice grew, so did the responsibilities thrust upon him by others. He served as Chief of Staff and Chief of Orthopaedics at Cobb Hospital and Medical Center, and at the Kennestone Windhill Hospital, both in suburban Atlanta. He served as President of the Cobb County Medical Society and Vice President of the Medical Association of Georgia. Currently, he is Vice Chairman of Georgia's delegation to the American Medical Association and will chair the delegation in 1997. He is a past President of the Georgia Chapter of the American Jewish Committee and served as Chairman of the Physician Section of United Way in 1988.

His varied activities outside of his regular occupation of orthopaedics brought Dr. Cohen to the attention of Leadership Atlanta, which he was invited to join in 1981. Leadership Atlanta is a network of 2,000 selected people with leadership qualities between the ages of 35 and 50 years whose sole purpose is to better the life of Atlanta. The group meets monthly for an entire day to discuss topics relevant to life in Atlanta, such as race relations, the justice system, and the media, among others. Networking within Leadership Atlanta provided the spark, commitment, and key contacts which ultimately resulted in Atlanta's successful bid for the 1996 Summer Olympic Games. Dr. Cohen was appointed a member of the Atlanta Olympic Organizing Committee in 1988, an appointment which signaled his official connection with the Olympic effort.

His real work as a member of the Atlanta Olympic Organizing Committee began after Atlanta was selected to represent the United States in the bid against other competing countries for the privilege of hosting the 1996 Summer Olympic Games. Dr. Cohen chaired the Medical Commission within the official Bid Committee for the 1996 Olympic Games. The job of the Medical Commission was to develop the medical concept for the International Olympic Committee (IOC) bid which had to include details for providing medical care for more than two million spectators, 12,000 athletes, 70,000 support personnel, and 15,000 media personnel. The responsibilities not only included the medical care of both athletes and spectators and medical care in the Olympic Village, but also mechanisms for gender verification and doping control of competing athletes.

Dr. Cohen was a member of the Atlanta group sent to Tokyo in 1990 for the final site selection to be made by the International Olympic Committee (IOC) between the six finalists, Toronto, Belgrade, Manchester, England, Melbourne, Australia, Athens, and Atlanta. To their joy, Atlanta was selected as the host of the 1996 Summer Olympic Games. Like the 1984 Los Angeles Summer Olympic Games, Atlanta's bid was privately funded. The American TV rights, the city's Southern charm, and Atlanta's presumed ability to make the Games a financial success are believed to have been important factors in Atlanta's selection. After the joy of success came the realization that now the hard work began for the Atlanta people. After returning from Tokyo, Dr. Cohen was appointed Chairman of the Third IOC World Congress on Sports Sciences and Chairman of the Doping Control Program for the 1996 Olympic Games, a responsibility which would still leave him some time for his practice.

Dr. Cohen soon learned that the science of modern doping control is based on analytical chemistry, an observation that necessitated brushing up on his knowledge of biochemistry. He also learned that most mistakes in doping control occur during the time between athlete notification and urine collection and

Dr. Cohen on site at the Games
with David Apple, Co-Chairman

its transport to the laboratory for examination. It became evident to the Doping Control Committee that the "chain of custody," or the tracking of the urine sample from the manufacturer of the sample collection kit, to the notification of the athlete, to the collection of the urine sample and its transport to the laboratory, must be made totally secure to prevent mistakes. In addition to employing a local bonded courier service for transport of the urine sample to the laboratory, his committee obtained special tamper-proof containers from England, made especially for this purpose. The Doping Control Program had to develop its own laboratory facilities in Atlanta, and also had to identify local, national, and international experts to assist in all the details of adequate and effective doping control.

During the Olympic Games, Dr. Cohen's Doping Control Program supervised a total of 23 different Doping Control Stations and 450 volunteer personnel. Dr. Cohen explains that because of the way events are scheduled during the Olympics, only about 18 of these stations operated at any one time. A Doping Control Station is where urine is collected from the athletes and where the "chain of custody" is most complicated. Dr. Cohen says they tested all medal winners and, randomly, about one in four other athletes. Those housed in the Olympic Village knew of the policy and were aware of the possibility of being tested. After each event, the winners have one hour in which to report to a Doping Control Station. This grace period gives the athlete sufficient time to attend the medal ceremony and press conferences. The "chain of custody" begins at this point because each medal winner is chaperoned closely after the finish of the event by a Doping Control Escort.

Each Doping Control Station is staffed by a team of physicians and paramedical personnel and each urine collection is observed by a staff person. After collection, the urine sample is split into two samples, A and B. Each is placed in a tamper-proof container and put into a secure transportation bag. Local bonded couriers deliver the samples to the testing laboratory run by the SmithKline Beecham Clinical Laboratory Service. Urine sample A is then analyzed for stimulants, narcotics, diuretics, anabolic steroids, and peptide hormones. In addition, Dr. Cohen's committee rented three high-resolution mass spectrometers which can not only identify minute amounts of steroid in a urine sample, but also can identify traces of steroid taken months before. Use of this high-tech testing tool in Atlanta was an Olympic first. The Doping Control Program's specific responsibility for the urine sample ends when the sample reaches the laboratory.

The result of each urine examination is reported within 24 hours to the International Olympic Committee (IOC) Medical Commission. If the test is positive for any banned substance, the athlete is informed and Sample B is then examined as a verification check. If sample B is positive also, the athlete is informed and given a chance to explain to the IOC Medical Commission which has the power to impose sanctions. In past Olympic Games, some sanctioned athletes sought injunctive relief from sanctions by pleading to local courts. This never proved to be a satisfactory solution for either the IOC or the sanctioned athlete because of variability within court systems around the world.

In 1994 the IOC instituted a new method for appeals by setting up an International Court of Arbitration which was used for the first time during the 1996 Games in Atlanta. In order to compete in the 1996 Games, each athlete had to sign an agreement not to appeal a sanction to a U.S. court but, rather, to take his appeal to the new International Court of Arbitration. This new appeals process is a totally independent mechanism with a main panel of 150 lawyer arbiters from all over the world. Each appeals panel consists of three lawyer arbiters drawn from the main panel. Sanctioned athletes appealing to this new Court of Arbitration can expect a binding decision within 24 hours.

Dr. Cohen and his committee hope their efforts during the 1996 Olympic Games in Atlanta will lead to a better doping control system for future Olympics and for all organized competitions. As Dr. Cohen explains, each country has its own Olympic Federation which sets the standards and guidelines for Olympic participation in its own country. Then, for a single two-week period during each Olympic Games, each international federation functions under IOC control. Dr. Cohen is hopeful that the 1996 Atlanta Olympics were a step toward greater cooperation among the 26 different federations. Considerable variety in standards and guidelines still persists among competing countries and sports federations, at least as far as doping control is concerned. Dr. Cohen believes that the different federations may become convinced of the advantage of adopting a better doping control system which is more standardized as to details of collection, analysis, and sanctions, such as the system employed in Atlanta for the 1996 Summer Olympic Games. ■

The Makings of the Compleat Physician

J. Edward Berk '36

Clinically oriented physicians, whether their time be spent in private practice or in clinical teaching in the halls of medical academe, come to identify certain fellow physicians who stand out from the rest. They possess certain qualities and attributes that command the respect and admiration of their colleagues. For want of a better term, I have categorized them as "compleat" physicians, purposely using the old spelling "compleat," after Isaak Walton's *The Compleat Angler* (1653).

The principal qualities that characterize the "compleat" physician may be defined and considered under several headings:

A Permanent Student

A basic attribute of the compleat physician is remaining forever a student. At the very beginning of his career he appreciates that being a student does not end with graduation from medical school. Thus does he insure that the remarkable and never-ending discoveries, the additions to and the modifications of our sum total of knowledge in the broad field of medicine will not go unnoted by him.

Inquisitiveness

To assure that he indeed maintains his student role, the compleat physician is driven by an unquenchable inquisitiveness and an insatiable curiosity. Always, as phenomena are encountered clinically or in the laboratory, he is moved to ask, why have these phenomena developed? How do they arise? By what mechanisms? He is fully aware that all of us command the same serving men of whom Rudyard Kipling boasted:

I keep six honest serving men
(They taught me all I knew).
Their names are What and Why and When
And How and Where and Who.

Alert to Gains from Serendipity

The compleat physician does more than remain an inquisitive student. He is alert as well to phenomena that appear purely by chance in the course of daily activities—phenomena that he was not purposely seeking. These, too, arouse his curiosity and invite his interest in their origin, mechanisms, and significance.

In a letter written by Horace Walpole in 1754 to his friend, Horace Mann, Walpole described how taken he was by a fairy tale he had recently read titled "The Three Princes of Serendip" (the ancient name of the land changed to "Ceylon" and presently known as "Sri Lanka"). The princes were distinguished by their uncanny knack of uncovering interesting findings for which they were not looking. Walpole felt that this remarkable capacity and its potential deserved to be incorporated in some way into the English language. To serve such a purpose, he suggested the word "serendipity." This suggestion was adopted and the word is now a fixture in our dictionaries and speech.

The gains from serendipity have added importantly, not only to the depth and breadth of general knowledge, but also to human welfare. Two outstanding examples are the observations of von Mering and Minkowski and those of Fleming.

In the late 1800s, little was known about the function of the pancreas. Two investigators, von Mering and Minkowski, sought to shed some light on this through a series of experiments testing the influence of the pancreas on various ingested food substances. As part of their experimental approach, they surgically removed the pancreas in a series of dogs with the intent of determining what alterations occurred in the digestive process as a consequence of having no pancreas. In a chance postoperative conversation with one of the animal caretakers, the caretaker offhandedly commented about the terrible time he was having fending off flies that would immediately swarm around areas in the ground where the dogs had just urinated. Von Mering and Minkowski, struck by this, verified the caretaker's observation. Suspecting that it might be explained by the presence of some substance in the urine of these dogs that was attractive to flies, they obtained urine from the dogs and examined the specimens. The striking finding that emerged was the presence in the urine of large amounts of sugar. Thus for the first time a specific organ was identified as involved in sugar metabolism and in some way responsible for diabetes mellitus. Out of this serendipitous finding ultimately came the identification of the pancreatic islets and the extraction from them of insulin.

The gain from serendipity made by the British microbiologist, Alexander Fleming, is likewise notable and exciting in its genesis. In 1929, Fleming examined a culture he had prepared of a virulent bacterium. He was dismayed to find that the culture had been contaminated by a mold whose overgrowth rendered the culture of little value. Just as he was

---

Adapted from the Joe Henry Coley '34 Lecture delivered by Dr. Berk at Jefferson Medical College. Dr. Berk is Distinguished Professor and past Chairman of Medicine at the University of California, Irvine, School of Medicine.

about to discard it, however, he happened to note that wherever the mold grew in abundance, there were no evident bacterial colonies.

To find some explanation for this phenomenon, he harvested the mold and prepared a pure culture of it in a broth medium. He then inoculated the broth culture of the mold with the bacterium that he was studying and found that bacterial growth was markedly inhibited. This suggested to him that some substance within the mold passed into the broth culture and suppressed the growth of the virulent bacteria. Since the class of the mold was "penicillium," he named the unidentified substance "penicillin." Thus was born the antimicrobial era in medicine.

I cannot conclude these remarks on the potential gains from serendipity without quoting one of the pithy comments of that great phrasemaker, Yogi Berra of baseball fame: "You can observe a lot by just watching." Yogi's expression probably says it all.

Investigation

The compleat physician is not content to be merely an alert observer. Inherent in the total makeup of such a person is a meritorious passion to seek answers to the questions raised by the phenomena he might purposely or purely by chance observe. It is of little moment how simple or how minor the investigative study he undertakes may be. Nor should the investigative attempt be viewed as nonproductive if the results are uninformative or non-contributory. Out of the attempt itself there will be gains with a salubrious effect on that physician's future approach to the management of his patients.

The investigative effort will at the least provide a better understanding of some of the principles of research. Among these is recognition of the importance of appropriate controls and the determination of what constitutes "significant" differences. Also will come appreciation of the enormous effort and time that is consumed in searching the literature for previous or related reports, in maintaining records, in assembling the data, in devising tables and illustrative material, in writing the report, and in supplementing the data with properly arranged references.

If the study should involve a review of hospital records, the physician will likely be moved from the experience to be more detailed thereafter in his own recorded depictions of the clinical features in a given patient. And the frustrations he may have experienced in trying to decipher written records will be apt to make him more sensitive to writing legibly. Engaging in an investigative effort will also make a physician more restrained when ordering a medication or a test; he will be more inclined to make certain that the information to be gained, or the benefit that may ensue outweighs the attendant risks.

It is a commonly held belief that research of any value requires a fully equipped laboratory, sophisticated and complex equipment, and a host of technicians with special skills and knowledge. To the contrary, simple, inexpensive, extremely modest clinical research carried out entirely alone, without benefit of supporting personnel and sophisticated equipment, may nevertheless contribute worthwhile information.

Consider the example of William Beaumont, dubbed by Osler the "backwoods physiologist." Beaumont was an Army surgeon stationed in 1822 at Fort Crawford, a remote post along the upper Mississippi. It fell to him to care for a trapper named Alexis St. Martin who had accidentally fired his rifle into his abdomen. Under Beaumont's patient care, St. Martin recovered but was left with a fistulous opening in his abdominal wall that communicated with the stomach and through which the interior of the stomach could be seen. Even though working alone, without previous experimental experience, and devoid of the paraphernalia that an investigator at that point in time would be expected to possess, Beaumont nonetheless set about observing and testing the digestive capacity of the stomach in St. Martin and carefully recorded his numerous observations. He even aspirated the gastric juice and verified that it was acidic.

For years he compiled and recorded careful observations, but refrained from submitting them for publication in a medical journal for fear they would be rejected or ridiculed. When he was finally persuaded to allow them to be published, some 16 years after the accident, he almost immediately attained international fame and won an honored and permanent place in medical history.

Flexibility

A hallmark of current-day medicine is the remarkable profusion of new evidence, new insight, new discoveries. Because of them, physicians must maintain what may be described as "intellectual flexibility." They must possess receptive minds, examining new data and findings critically but being prepared, should these data prove convincing, to alter, modify, or even discard previously held concepts and ideas. They must constantly rethink, reappraise, reevaluate, or un-learn much of what they learned in medical school as newer information may dictate. Walter B. Cannon, M.D., the distinguished Harvard gastrointestinal physiologist, expressed the need for intellectual flexibility in these well stated words: "We dwell in a world which is not settled, not stationary, not finally immobilized. Consequently, wisdom counsels keeping our minds open and recipient, hospitable to new views and fresh advances" (*The Way of An Investigator,* 1945). We must avoid what John Stuart Mill called "the deep slumber of a decided opinion." Josh Billings (the pen name of a popular humorist of yesteryear) also underscored the danger inherent in a frozen mind or a fixed idea in one of his classical aphorisms: "It's not

what we don't know that gets us into trouble. It's what we know that ain't so."

Humility

The compleat physician is characterized by humility. He is the first to acknowledge that his diagnostic and therapeutic triumphs are not entirely of his own making. He is aware and appreciative of the fact that contributions by others helped make his own successes possible: the microbiologist who identified the responsible organism and assessed its sensitivity to various antibiotics; the pathologist whose microscopic examination of tissue revealed abnormalities that established the nature of the disease; the radiologist whose interpretation of images provided insight into the extent and nature of the underlying disorder; the endoscopist who supplied visual depictions of directly visualized lesions as well as biopsies that aided diagnosis; and the nursing staff whose tender and devoted care contributed enormously to the patient's ultimate recovery.

Attitudes and Relationships with Patients

That medicine is both a science and an art and not a pure or an exact science soon becomes evident to all physicians who are clinically engaged. None appreciates this more, however, than the compleat physician. All the modern-day, sophisticated diagnostic approaches notwithstanding, he does not abandon the fundamentals of a carefully taken history with a reasoned clinical interpretation of the symptoms, followed by a carefully performed physical examination. He does not succumb to the current error of "five minutes of history and five days of testing."

The compleat physician is also mindful that certain elements, attitudes, and feelings deeply influence the relationship between physician and patient. Time and again he has noted that open display of these feelings seems to contribute more to the well-being of his patient than do the medications he prescribed or the various other therapeutic measures he may have employed. These basic emotions and attitudes encompass "compassion," "concern," and "caring."

In the early part of the present century, Francis Weld Peabody, M.D., Professor of Medicine at Harvard, said in a discourse on the care of the patient that "the secret of the care of the patient is in caring for the patient." These words should be engraved on the hearts of every physician as they certainly are on those who qualify as compleat physicians.

The quintessential attributes of "compassion" and "concern" are portrayed in the painting *The Doctor* by Sir Luke Fildes. The scene is set in 1891. It depicts a physician, garbed in the dress of that day, gazing intently at a very sick young girl who lies before him on a makeshift bed. In the background are a weeping mother and a consoling father. Strikingly captured by the artist are the troubled emotions churning within the doctor: compassion and concern as he gazes at the sick; frustration and perhaps even anger at his inability to do anything truly effective. Even the most recent of today's medical school graduates could enter this home-based scene, whip out a syringe filled with a potent antibiotic, inject the contents into the sick young girl, and then leave without so much as a consoling word to the distraught parents, yet rest content that by the following morning the chance is great that the child will show improvement. Were any physician to perform in this fashion, however, he would, despite the superior effectiveness of his treatment, be far surpassed in human qualities by the frustrated physician shown in the painting.

All too often physicians must deal with situations in which everything currently known or available has been tried but without success. The disorder from which the patient suffers progresses inexorably and a fatal outcome is inevitable. In such situations, it does not suffice to simply pronounce the imminence of a fatal outcome and with that to depart, leaving the distressed family bewildered and emotionally torn. The true and compleat physician needs no reminder that in such trying circumstances he must in some way provide consolation and support even though he too is tormented and emotionally anguished.

What may be the best human compassion at such sad times is illustrated in a little story that I came across some time back. A young mother is anxiously awaiting the return of her son from school. With each passing minute she grows more and more concerned. Finally, the young lad appears. Seeing at a glance that he is uninjured, she gives vent to her pent-up emotions by berating him for his tardiness. The lad looks at his mother and says, "Jim's bike broke down and I had to help him." This explanation only rekindles the mother's agitated state: "Help him! How could you help him? You know nothing about fixing bikes." Again the youngster looks meekly at his mother and says: "You're right, mom, I don't know how to fix a bike and I couldn't help Jim fix his. But, mom, I had to help him cry."

This is precisely what the compleat physician will attempt in such emotion-draining situations. He will try as well as he can to console a troubled family and friends, and help them cry.

Inscribed on the statue of Dr. Edward L. Trudeau, a pioneer in the treatment of tuberculosis, is a 15th-century (or perhaps earlier) folk saying. The last three words succinctly express the warmth of the compleat physician that I have been attempting to describe: "To cure sometimes, to relieve often, to comfort always."

❧

I hope that my young colleagues-to-be will aspire to become "compleat" physicians. Should you succeed, I would say to them, in incorporating into your every action those attributes that characterize a physician of this quality, then, at the end of your career, you will have the rewarding satisfaction of knowing that your life in medicine was a noble one, a contributory one, one that won for you the love and appreciation of your patients and the respect and admiration of your colleagues.

Jefferson Health System and Mercy Health Corporation Forge Major Alliance

Mercy Health Corporation of Southeastern Pennsylvania and Jefferson Health System have announced plans to form a comprehensive alliance. Plato A. Marinakos, President and Chief Executive Officer of Mercy, and Douglas S. Peters, President and CEO of Jefferson Health System, signed a Memorandum of Understanding between the two health care delivery systems following approval by their respective governing boards. As a result of this alliance, Mercy and Jefferson will form a new, integrated, multi-institutional health network with broad geographic coverage of the Delaware Valley.

"Through this alliance, Mercy seeks to partner with Jefferson Health System to enhance and strengthen our mission," says Marinakos. "Our collaborative efforts will build on Mercy's 80-year health care tradition as well as Jefferson's long-standing commitment to the health needs of the community. This includes a shared commitment to serve all, including those in the greatest need."

Health care services offered by Mercy and Jefferson span the entire Delaware Valley. This alliance will enhance existing programs and services and create new joint initiatives through a separate joint services organization in order to meet the health needs of the region. Alliance initiatives include program development in primary care, ambulatory care centers, physician networks, home health, rehabilitation, behavioral health, long term care, and managed care.

"Specifically, we will bring together the complementary resources of Mercy, which has its foundations in community-based ambulatory and acute hospital care services as well as managed care expertise, with the primary, tertiary, community, and academic strengths of Jefferson," explains Peters. "Drawing on our expertise and knowledge, we will meet the challenges faced by the health care industry with innovative programming solutions."

The Mercy-Jefferson alliance will link two of the larger health care systems in the region including a network of more than 2,700 hospital beds and more than 3,000 physicians. As Marinakos explains, "The purpose of the alliance is to focus on a vision of the future of health care where services are delivered in very different ways than they are today. Toward that vision, we will develop a broad range of joint services including linking our respective home health organizations to create the largest provider of its kind in the area, establishing a wide network of ambulatory care centers, integrating our physician networks, investing in long-term care and chronic care, and realigning our acute hospitals to face the future under managed care."

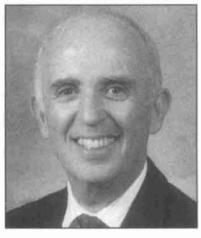
Additionally, it is the objective of the alliance to resume an academic affiliation between Mercy and Thomas Jefferson University in support of residency programs at Fitzgerald Mercy and Misericordia Hospitals. Mercy was a major teaching affiliate of Jefferson from 1969 to 1991.

System assets will not be merged, and individual system identities will be maintained. The Memorandum of Understanding calls for Mercy and Jefferson to develop a definitive alliance agreement by April 30, 1997.

Peters explains, "The strengths of Mercy and the Jefferson Health System complement one another. We are very pleased and excited to have Mercy join Jefferson as a major partner. This alliance creates tremendous depth of service and broad coverage, offering a complete continuum of care to the Delaware Valley region."

"Mercy will continue to preserve and expand the Catholic health care ministry of our sponsors, the Sisters of Mercy," says Marinakos. "The Jefferson Health System philosophy is consistent with our mission and values as an organization. Our cultures and styles are similar, and Jefferson shares our commitment to caring for the health needs of the community. Together we will respond to the future of health care in creative and proactive ways."

Schwartz Joins Pediatric Faculty



Elias Schwartz, M.D. has been appointed Director of Medical Research in the Department of Pediatrics at Jefferson Medical College and the duPont Hospital for Children in Wilmington, a close affiliate of Jefferson. He comes to Jeff from the Children's Hospital of Philadelphia, where he was Physician-in-Chief and Chairman of Pediatrics.

Dr. Schwartz has written more than 200 papers on blood disorders of children, including the genetics and treatment of hemoglobin abnormalities such as thalassemia and sickle cell disease. He has lectured extensively on anemia, bleeding and platelet disorders, and the molecular biology of hereditary blood abnormalities. He is a past President of the American Society of Pediatric Hematology/Oncology.

Partial Liquid Ventilation Helps Premature Infants to Survive

Jeff physicians, in collaboration with pediatricians from institutions across the United States, have discovered that partial liquid ventilation, also known as perfluorocarbon associated gas exchange, leads to clinical improvement and survival in some infants who were not predicted to survive due to respiratory distress syndrome. These findings appeared in the September 11 issue of *The New England Journal of Medicine.*

The research builds upon previous studies of the efficacy of liquid ventilation, which uses a perflubron liquid called LiquiVent® from Alliance Pharmaceutical Corp., San Diego and Hoechst Marion Roussel. The odorless, colorless, and biologically inert chemical is used to gently expand and oxygenate lung air sacs of premature infants who are in respiratory distress. By introducing LiquiVent® via glass syringe into the infant's endotracheal tube and keeping the substance oxygenated in the lungs with a ventilator, the research team showed that partial liquid ventilation is as effective in infants as it has proven to be in animals. "Liquid ventilation more naturally simulates the fluid-filled condition of lungs before birth," explained co-author Jay Greenspan, M.D., Associate Professor of Pediatrics at Jefferson.

The study focused on 13 premature infants (gestational age 24 to 34 weeks; birth weight 600 to 2000 gm) less than five days old with severe respiratory distress syndrome who had failed conventional therapy including surfactant. Infants were ineligible if they had conditions that would interfere with the interpretation of outcomes or render medical intervention futile.

Within one hour of beginning partial liquid ventilation, oxygenation improved and chest radiographs revealed even expansion of the lung air sacs. Infants were weaned to gas ventilation without complication. Eight of the 13 infants survived to at least 36 weeks corrected gestational age.

"The implications of this study are far-reaching," comments Dr. Greenspan. "We now have further evidence that partial liquid ventilation with LiquiVent® is a safe, lifesaving option for premature infants who had virtually no chance of living before the advent of respiratory therapies."

Dr. Greenspan's contributions to this study follow years of his and Jefferson's devotion to studying liquid ventilation and other respiratory therapies. Jefferson was the first Philadelphia-area hospital to offer extracorporeal membrane oxygenation (ECMO), a surgical bypass procedure that uses a heart-lung machine to oxygenate and circulate blood. These previous studies and breakthroughs make Jefferson an ideal primary site for an upcoming Phase II study of partial liquid ventilation.

Plectin Protein Deficiency is a Hereditary Basis for Muscular Dystrophy with Epidermolysis Bullosa

Researchers from Jefferson Medical College, in collaboration with investigators from the United Kingdom, have cloned and sequenced a gene which underlies a subtype of epidermolysis bullosa (EB), a severe, inherited, blistering skin disease, and which is associated with late-onset muscular dystrophy. These findings were published in the August 1 issue of *Nature Genetics.*

The findings suggest that a defect or deficiency in plectin, one of the proteins involved in anchoring skin layers, appears to underlie EB and muscular dystrophy. According to Jouni J. Uitto, M.D., Ph.D., Chairman of Dermatology and Cutaneous Biology, the study results are significant because they demonstrate that EB affects muscle in addition to the layers of skin. The new information will allow for early diagnosis of muscular dystrophy in infants born with skin blistering as well as provide DNA-based prenatal testing for the disease.

The study focused on four families with members born with EB and who later developed muscular dystrophy in the second decade of life. At birth, these patients were noted to have skin blisters characteristic of EB. Years later they complained of muscle weakness. Without scientific evidence, a relationship between EB and muscular dystrophy could only be considered coincidental. "Our study was designed to see if there was a connection between epidermolysis bullosa and muscular dystrophy," explains Dr. Uitto. "Study results lead us to believe that EB is a warning sign of muscular dystrophy in some people rather than an unrelated disorder."

By studying patients with the autosomal recessive disorder termed epidermolysis bullosa with muscular dystrophy (EB-MD), researchers found that plectin is absent in these people. The absence of plectin suggests that it is the candidate gene/protein system for EB-MD mutation and led investigators to clone and sequence the human plectin cDNA.

As a result of the research findings, women who have a child with EB-MD are eligible for prenatal testing via chorionic villi sampling during the ninth week of their subsequent pregnancies.

The study was truly a multinational effort, joining the talents of Jefferson researchers and investigators from the University of Dundee; St. John's Institute of Dermatology, London; Queen Mary and Westfield College, London; ICRF Clare Hall Laboratories, Hertfordshire; the University

continues at right

"Gene Repair" Technology Corrects Genetic Mutation Leading to Sickle Cell Anemia

Researchers at Thomas Jefferson University have demonstrated a new gene repair technology that may hold promise as a treatment for sickle cell anemia and other diseases by correcting the DNA mutation from which they arise. In a study published in the September 6 issue of *Science,* researchers led by Eric Kmiec, Ph.D., Associate Professor of Biochemistry and Molecular Pharmacology, report the use of therapeutic sequences of genes, termed chimeraplasts, to correct the specific point mutation that causes sickle cell anemia. Based upon this and other research already underway, the investigators theorize that chimeraplasty may one day provide an effective treatment for an array of diseases that have a similar genetic basis as sickle cell disease.

The team of scientists from Jefferson's Kimmel Cancer Center, Cooper Medical Center (Camden, New Jersey), and Cornell University School of Medicine introduced the chimeraplasts into blood cells drawn from a sickle cell anemia patient. Sickle cell anemia arises from a hereditary mutation in the β-globin gene. Chimeraplasty corrected the mutation in up to 10 to 20 percent of the blood cells in the sample; a level which the experts believe can potentially alleviate painful symptoms and help to prevent the systemic organ damage caused by the disease. The researchers found that the frequency of correction in cell samples was dependent on the amount, or dose, of chimeraplasts used.

"With this gene repair technique, we hope to correct the genetic mutation in human blood cells in sufficient quantities to fortify the population of normal, healthy blood cells in sickle cell anemia patients and reduce the episodes of pain and organ damage," says Dr. Kmiec. "In addition, chimeraplasty may represent a promising new therapeutic technique to correct known mutations that cause other genetic diseases, such as cystic fibrosis and Gaucher's disease."

Future clinical studies to evaluate the safety and effectiveness of chimeraplasty in sickle cell patients would involve drawing blood from a patient and then introducing chimeraplasts into the blood's stem cells. Stem cells are precursors from which the body's red and white blood cells arise. The investigators theorize that by correcting the β-globin mutation in these early stage cells, the correct DNA sequence will be expressed in all subsequent blood cells. Therapy would most likely conclude with implantation of the corrected cells back into the patient via a bone marrow transplant.

Chimeraplasty may be a very important development in the field of gene therapy, which is divided into two categories. The first is known as gene augmentation. These drugs compensate for the disease state by incorporating a correct copy of a gene into a diseased cell, which then expresses the normal protein and compensates for the deficiency. The second category, which includes chimeraplasty, is known as chromosomal targeting, or gene correction. These drugs aim to correct or eliminate a given gene from within the chromosome of the diseased cell. "The ability of any vector to target a single base that is incorrect in a particular gene is particularly challenging," says Dr. Kmiec. "But the effort is essential because, if achieved, it will provide a number of clinical advantages."

One important advantage is that no extra DNA is introduced into the cell, so the gene may be corrected within the context of its normal chromosomal environment. Also, gene correction may require fewer doses, or even only a single dose, until an adequate percentage of cells are corrected. Finally, an immune response to the drug can be avoided since the gene that is corrected is a natural component of the cell.

In sickle cell anemia, the β-globin gene mutation leads to the production of red blood cells that are banana- or sickle-shaped, and rigid in the presence of low oxygen, whereas normal red blood cells are round and flexible. The odd-shaped cells may become stuck in the capillaries, pile up, and cut off blood flow to tissues. Oxygen deprivation of tissues can lead to severe episodes of pain, known as crises. In addition, the misshapen cells only live for about 20 days and are destroyed when trapped in the liver and spleen. This results in anemia.

Sickle cell anemia is the most common form of sickle cell disease, and affects more than 50,000 Americans. Most cases occur among African-Americans, although it is also common among persons of Arabian, Caribbean, East Indian, Mediterranean, and South and Central American descent. About one in every 400 to 600 African-Americans inherits sickle cell disease.

EB, *from left*

of Marburg; Citta University, Catania; St. Luke's Hospital, Malta; Nagoya University; and the Vienna Biocenter, Vienna.

Dr. Uitto's contributions to this multinational effort follow years of devotion to studying EB. In 1991, he helped identify a collagen gene responsible for holding skin together and linked a site on the gene to a form of EB. This research provided a foundation for the EB-MD study.

Genetic Discoveries Lead to New Tests for Lung Cancer

Cancer researchers led by Antonio Giordano, M.D., Ph.D., of Jefferson's Kimmel Cancer Institute, believe that damage to *Rb-2/p130,* the human retinoblastoma-related gene, may lead to lung cancer. Cigarette smoke, air pollution, some toxins breathed by workers, and other environmental carcinogens may cause the damage and inhibit the body's ability to make the *pRb-2/p130* protein, a powerful tumor suppressor in humans and mammals.

The investigators are already creating a new lung cancer early detection and tumor-grading test to enable physicians to assess how much protein from *Rb-2/p130* is found in individual lung cancer patients. Based on the results, clinicians may begin treatments earlier and tailor them according to how aggressive the cancer is. This finding, which appeared in the July issue of *Clinical Cancer Research,* is the latest for the Jefferson team and collaborators from the departments of anatomic pathology and respiratory disease at the Second University of Naples. The work was funded primarily by the National Cancer Institute (NCI).

"Dr. Giordano's findings have the potential to reduce mortality from lung cancer significantly," notes Dr. Arthur C. Upton, former Director of the NCI and President of the Ramazzini Institute. "By identifying the molecular nature of the changes causing cancer in cells of the lung, his findings may lead to tests for the early detection of such changes and to strategies for preventing and for successfully treating the disease."

Clinical application of the researchers' laboratory work, and the publication this spring of *Rb-2/p130* studies in three prominent medical journals, mark an important culmination point in the study of the retinoblastoma gene's involvement in cancer. Dr. Giordano has been studying the gene for eight years.

"Based on the fact that *Rb-2/p130* protein levels correspond with the stage of lung cancer, a new test to measure the levels could be an immediate benefit in determining how aggressive cancer tumors are in individual patients," says Emanuel Rubin, M.D., the Aponte Professor and Chairman of Pathology, Anatomy, and Cell Biology, who is collaborating with the research team on development of the test.

In a previous paper in the May 1 issue of *Cancer Research,* Dr. Giordano's team identified the gene named *Rb-2/p130,* located on chromosome 16, and showed that it makes a protein that plays a vital role in controlling the cell cycle in all human and mammalian cells. When *Rb-2/p130* is altered and cannot produce its protein, *pRb-2/p130,* the cell may not reach the natural stage of programmed cell death. Instead, the cell continues to live and divide out of control possibly leading to tumor formation and cancer.

In tests of various cancer cell lines, when normal (wild type) *pRb-2/p130* was reintroduced back into cancerous cells, the protein interacted with several other proteins, most notably one named cyclin A, to block uncontrolled cell growth by moving the cell along to the next stage in its natural life cycle, which eventually ends in apoptosis. Without the critical tumor suppressor gene, the cells continued to live and divide.

The scientists next published the complete DNA makeup of *Rb-2/p130* in the May 15 issue of *Proceedings of the National Academy of Sciences.* "Since we observed in the lab that a lack of *pRb-2/p130* may play a critical role in prolonging cell life in a variety of cancer types, learning about the gene's complete genomic structure and sequence would even better enable us to understand how *pRb-2/p130* works so that we could focus our efforts towards a clinical intervention in patients to either prevent them from developing cancer, or to kill cancer tumors already developed," says Dr. Giordano.

A practical opportunity to apply this work to the diagnostic realm of cancer medicine soon arose. In the July issue of *Clinical Cancer Research,* Dr. Giordano's team described a study of 77 tumor samples from male and female patients with surgically resected lung cancer. They found that the less the *pRb-2/p130* protein is expressed by a tumor, the more aggressive the lung cancer. In normal lung cells, a high amount of *pRb-2/p130* is present. This data opens the door to developing a variety of tests against the complete pathogenesis of lung cancer in patients.

The first type of test should be widely available within two years. The test will accurately describe which stage of cancer, either I, II, III, or IV, that individual patients are in, based upon the levels of *pRb-2/p130* that are present in their excised lung cancer tumor. Treatments may then be tailored accordingly.

Another test type now being investigated aims to analyze *Rb-2/p130* in individuals to determine genetic susceptibility to lung cancer.

Yet another type of test being investigated will use the *Rb-2/p130* protein as a tumor marker to learn when patients have developed lung cancer.

"Using *pRb-2/p130* as a tumor marker may be an efficient method of continuously monitoring the group of patients who is at the greatest risk for lung cancer before any morphological changes have occurred in the lung," says Dr. Giordano. "In addition, the ability to determine the exact level of *pRb-2/p130* expression in individual lung cancer patients may be a powerful prognostic tool for physicians to aid them in determining the most appropriate treatment strategy. Now that we recognize an inverse correlation between *pRb-2/p130* expression and lung cancer stage, the questions

are: what levels of *pRb-2/p130* expression show cancer? And what levels of *pRb-2/p130* expression correlate with each stage of lung cancer? These answers will be found through a large-scale screening of patients."

Such a study is now underway. The test, which will be a surrogate to histological grading by a pathologist, is now under development in a collaborative effort between Jefferson's Departments of Microbiology and Immunology, and Pathology, Anatomy, and Cell Biology.

Another important application of a test for *pRb-2/p130* may be the ability to determine earlier than previously possible susceptibility in groups at risk for lung cancer, such as ex-smokers and workers who have been exposed to airborne carcinogens. Foundry workers and people who live in highly industrialized areas often breathe high levels of combustion products, including carcinogens known as polycyclic aromatic hydrocarbons, which have been linked to lung cancer.

The Ramazzini Institute for Occupational and Environmental Health Research is a longtime supporter of Dr. Giordano's research. The institute is a nonprofit organization that promotes and coordinates multinational research and education.

Sheldon W. Samuels, Vice President for Policy Studies

continues at right

Selective Marker for Metastatic Colorectal Tumors Will Bring New Methods of Diagnosis

Researchers at Jefferson have discovered that the protein guanylyl cyclase C (GCC) is expressed in humans solely in the intestines, including the colon and rectum, making it a selective marker for colorectal tumors that metastasize outside the intestines. These findings appear in the December 10 issue of *Proceedings of the National Academy of Sciences*.

The research, led by Scott A. Waldman, M.D., Ph.D. (see page nine), Associate Professor of Medicine and Acting Director of the Division of Clinical Pharmacology, is groundbreaking because it has the potential to lead to the first effective way of detecting colorectal tumors once they migrate out of the intestines.

"The survival rate for patients who have metastatic colorectal cancer is presently very poor, with only five percent surviving after five years, because there has not been an effective way of tracking its spread to other organs and present chemotherapy does not make an enormous impact," explains Dr. Waldman. "Knowing that GCC is specific to the intestines allows us to use it as a tag or marker to detect where the cancer has spread."

By examining human tissue samples with the reverse transcription-polymerase chain reaction (RT-PCR), researchers discovered that GCC is only expressed by two different cells in the body. It is present in the single layer of cells that lines the normal intestine and continues to be expressed after these cells undergo malignant transformation and migrate out of the intestines into other sites. As a result of this, GCC acts as a marker, demarcating the cancer's spread throughout the body.

GCC is also the receptor for the heat-stable enterotoxin (ST) produced by E. coli. With this working knowledge, the Jefferson team exposed preparations of human tissues to ST and discovered that the only tissues that interact with this small protein were those that expressed GCC. Only tissues outside the intestine, containing metastatic colorectal cancer, expressed GCC and interacted with ST.

"We found that ST effectively binds to GCC in all tissues which contained metastatic colorectal cancer, regardless of the type of tissue or its location," says Dr. Waldman. "It is our hope that this research leads to new treatments that use ST as a guided missile to guide cancer-fighting poisons directly to metastatic tumor cells, without harming normal surrounding tissues."

Targeted Diagnostics and Therapeutics, Inc., a biotechnology company which has acquired the worldwide exclusive license to the work from Dr. Waldman's laboratory, is laying the groundwork for the birth of new diagnostic and therapeutic options by developing a tissue biopsy test that will accurately stage patients, to determine if colorectal cancer has spread outside the intestine. The company is also developing a blood test that will determine if colorectal cancer has spread beyond the intestine or has recurred after definitive surgery. In addition, work has begun on new therapeutics which will use ST to target and kill metastatic colorectal cancer cells.

"It is our goal to make diagnostic tests available for clinical use in the next two to three years, reducing the number of lives colorectal cancer claims each year, which is currently close to 50,000," says Harry A. Arena, C.P.A., M.B.A., President and CEO of Targeted Diagnostics and Therapeutics, Inc.

---

of the Ramazzini Institute and former chair of the Committee on Cancer Risk Assessment of the National Cancer Advisory Board, says, "Dr. Giordano's discovery may have a profound impact on the assessment of cancer-causing agents in the environment, by enabling regulators to measure risks to populations and individuals from specific doses of gene-damaging agents at the first stage of cancer development."

This is the second gene this year that has been linked to the development of lung cancer by researchers at Jefferson's Kimmel Cancer Institute.

HIV-1 Integrase Can Be Targeted for Gene Therapy

Researchers in the Division of Infectious Diseases have made two more important discoveries about the human immunodeficiency virus (HIV).

HIV-1 Envelope Has Permeable Pores

Researchers have discovered that individual, biochemically active HIV-1 viruses have permeable pores that make the HIV-1 envelope vulnerable to certain compounds designed to kill the virus. These findings were published in *Proceedings of the National Academy of Sciences.*

The research, led by Roger J. Pomerantz, M.D., Professor of Medicine, Chief of the Division of Infectious Diseases, and Director of the Center for Human Retrovirology, and Hui Zhang, M.D., Ph.D., research associate, is groundbreaking because it demonstrates that contrary to previous thought, the HIV-1 envelope is "open," allowing researchers to target and kill each individual virus with a group of compounds called nucleoside analog triphosphates.

"These compounds have the ability to penetrate the viral envelope, incorporate into and directly terminate the life of the virus," explains Dr. Pomerantz. "As a result, viral infectivity is potently inhibited."

Demonstrating these newly-found characteristics of the viral envelope has led Jefferson researchers to propose that nucleoside analog triphosphates might also directly act as virucidal agents that might be quite useful in preventing either heterosexual and / or homosexual transmission of HIV-1. These virucidal agents could be coadministered with spermicidal agents. Instead of only killing sperm, this formula would also kill the individual HIV-1 viruses before they became infectious.

"It is important to remember, however, that while this finding is extremely encouraging, it is not a cure for HIV-1 or AIDS," says Dr. Pomerantz. "In the short term it is our goal to use findings such as these to change AIDS from an acute disease to a chronic, treatable one."

HIV-1 Integrase Can Be Targeted for Gene Therapy

Jefferson scientists have discovered that intracellular immunized cells have the potential to inhibit the progression of the HIV-1 life cycle when used as therapy during integrase, the period of productive viral replication. These findings appear in the December issue of the *Journal of Virology*.

The research, led by Dr. Pomerantz and Drs. Lingxun Duan and Pnina Levy-Mintz, is groundbreaking because it is one of the first time that the integrase area of the viral life cycle has been targeted for therapeutic treatment. Integrase had been the most difficult, and is a most important, stage of HIV-1 to target with therapy.

"Being able to target integrase molecules, those that carry HIV-1 DNA into host cell DNA, can ultimately prevent the HIV-1 virus from spreading to new cells in patients already infected with the virus," explains Dr. Pomerantz.

This is the beginning of gene therapy research at Jefferson for treating HIV-1 infection. It brings basic science from the bench to the bedside.

Less Radical Treatment May Eliminate Breast Cancer

A study of women with in situ (noninvasive) ductal breast cancer reveals that excision and surveillance alone are an alternative to mastectomy or irradiation in treating noninvasive breast cancer. Results of the study were presented at the 32nd Annual Meeting of the American Society of Clinical Oncology.

The data, collected between 1975 and 1994 at Jefferson Medical College, shows that only 28 of 194 breasts (three women had bilateral in situ cancer) treated with excision and surveillance alone had a recurrence. There was a mean and median follow-up of 55 and 53 months, respectively.

During that time, only five of the 194 breasts in 191 women, or three percent of the recurrences showed evidence of invasive (or life-threatening) cancer, including microinvasion. Twenty-three recurrences were entirely noninvasive.

According to senior author and presenter Gordon F. Schwartz, M.D., M.B.A., Professor of Surgery at Jefferson and a specialist in diseases of the breast, these findings are contrary to those in most other studies to date. "No patient in this group has died from breast cancer since the study began," he explains. "Even if recurrence does take place, it is most likely to be the same type of noninvasive cells as the first time. And in selected cases, a second, local excision may be suitable instead of irradiation or mastectomy."

Women with a confirmed diagnosis of noninvasive breast cancer underwent post-biopsy mammography to verify excision of calcifications. Wide, local re-excision was performed in most patients. The maximum diameter of calcifications considered suitable for this treatment option was 2.5 cm.

"Excision and surveillance is a reasonable alternative to mastectomy or irradiation for selected women with in situ, ductal breast cancer that presents nonpalpable calcifications, or as an incidental finding," says Dr. Schwartz. "A major treatment recommendation such as radiation or mastectomy may be withheld until and if a recurrence does take place."

Dr. Schwartz notes that even if a recurrence does occur, it is likely to be noninvasive.

Melanoma Vaccine Clinical Trial Shows Significant Improvement in Four-Year Survival

Interim results from a clinical trial of a vaccine for treating melanoma, led by David A. Berd '68 of Jefferson's Division of Neoplastic Diseases, show significant improvement in four-year survival compared to currently available treatments.

According to the study, which will be partially disclosed on May 21 at the annual meeting of the American Society of Clinical Oncology, 62 patients were treated with a special vaccine made up in part of their own tumor cells. Four-year survival was higher than a control group of patients treated with standard surgery, and higher than patients who recently participated in studies of the drug alpha interferon.

The vaccine under investigation is being used postsurgically for treating advanced, but surgically resectable, malignant melanoma. In the study, patients with stage-III tumors in the lymph nodes were treated with the vaccine after standard lymphadenectomy—an operation where the melanoma and surrounding lymph nodes are removed. Of 62 patients who received the vaccine, 47 percent were free of relapse after four years, and 58 percent survived four years. This is compared to 20 to 25 percent survival in patients treated with surgery alone.

"The melanoma vaccine is made from a patient's own tumor cells, which are inactivated and modified with the chemical hapten dinitrophenyl. This process makes the tumor cells appear foreign to the patient's immune system, and so the immune system attacks and kills the cells," explains Dr. Berd. The patients also receive a low dose of cyclophosphamide, a medication commonly used in cancer chemotherapy, but which has been shown to boost the immune system when administered in the right way.

An unexpected finding was the significantly better survival of older patients in the study. The four-year survival of patients over 50 years old was 66 percent, compared to 46 percent for patients under 50.

Dr. Berd is also researching the application of this type of vaccine against other carcinomas, such as breast cancer, colon cancer, and ovarian cancer. These studies are scheduled to begin in about one year.

In recent years, mortality from melanoma has been increasing. In 1995, the National Cancer Institute (NCI) expected more than 34,000 new individual cases of melanoma in the United States alone, and expected almost 7,200 individuals to die from the disease. The incidence has increased nearly 80 percent between 1973 and 1987, at a rate of approximately four percent per year, according to the NCI.

Research Funding Keeps Growing

Jefferson received a total of $75.2 million in Federal and non-Federal research awards during fiscal year 1996, up from $72.1 million in fiscal year 1995. In 1995 it ranked 36th among the 124 medical schools in the United States in terms of research funding from the National Institutes of Health.

Critical Care Trials Group is Funded by NIH

Jefferson is one of 10 clinical sites nationwide selected to participate in the Critical Care Trials Group funded by the National Institutes of Health. "This marks the first time the NIH has supported a coordinated group of academic centers to design and carry out clinical trials in the areas of acute respiratory failure, sepsis, and critical care," according to Jonathan Gottlieb, M.D., co-principal investigator and Associate Professor of Pulmonary Medicine and Critical Care. "As part of the Critical Care Trials Group, we have the opportunity to offer our patients participation in the most advanced treatment protocols, as well as to enhance our state of knowledge."

Linear Accelerator for Radiosurgery at Wills Eye

Physicians at the Neurosensory Institute, Wills Eye Hospital, who hold faculty appointments at Jefferson Medical College, are performing brain surgery with a new device: a linear accelerator specially designed for stereotactic radiosurgery to the brain. With this technology they are treating both benign and malignant brain tumors, arteriovenous malformations, and intracranial disorders, noninvasively and on an outpatient basis.

Associate Professor of Neurosurgery David W. Andrews, M.D. explains that the new stereotactic treatment system delivers focused radiation in either a single dose, or in multiple fractions over a period of days. In either case, the patient usually returns to his normal routine within days and is spared the surgical trauma and side effects associated with open brain surgery.

Alumni Too Can Participate in JeffHOPE

JeffHOPE, the student-run homeless clinic and urban health care project which was featured in the June 1996 *Bulletin*, welcomes the participation of Jefferson graduates as well as students.

What Does JeffHOPE Do?

✔ provides free, accessible medical care to medically underserved individuals in Philadelphia

✔ provides social service information and counseling to patients at the clinic sites

✔ helps Jefferson students, staff, faculty, and alumni to educate themselves about the health problems and social service needs of the homeless and medically underserved, and the broader socioeconomic issues related to "health"

✔ conducts research into the health status and health needs of the populations JeffHOPE serves

✔ teaches formerly homeless patients about the health care system, health maintenance, violence prevention, and stress management

✔ gives students an opportunity to practice their history-taking, physical exam, and differential diagnosis skills while providing service to the community

What Does JeffHOPE Need?

✔ *Time*

JeffHOPE runs on the volunteer time of students and physicians. We need ***local primary care physicians*** to serve as preceptors at the clinics, and ***specialists in Philadelphia*** who are willing to accept a limited number of referrals from the clinics on a pro bono basis.

✔ *Supplies*

The clinics are supplied by donations from Thomas Jefferson University, drug companies, and private physician practices. The clinics need samples of commonly used drugs, dressing supplies, office equipment such as exam tables, blood pressure cuffs, and other medical supplies.

✔ *Financial Support*

JeffHOPE is a volunteer organization. The expansion of its services and opportunities has created an expansion in its operating budget. Funds are needed to support its service learning program, to continue its lecture series, to improve its patient education program, and to provide administrative support.

If you would like to help JeffHOPE to maintain its successes and expand its horizons, please call the JeffHOPE office at ***215 955 1878***.

JeffHOPE (Health Opportunities, Prevention, and Education) provides comprehensive health care through weekly clinics at shelters and service sites for underserved men, women, and children in Philadelphia. Since January 1993, JeffHOPE volunteers have been operating a primary health care clinic at St. Columba's shelter for homeless men. In November 1993, the volunteers established an additional clinic at Gateway Service Center, a city shelter and day program. A third shelter site opened in September 1996 at a needle exchange program site run by Prevention Point Philadelphia. Under consideration is a fourth site which would serve homeless and mentally ill women in Philadelphia.

All the clinics are staffed by volunteer physicians, residents, medical students, nurses, nursing students, and occupational and physical therapists. They work together as a team to provide health care for the poor and underserved men and women of Center City. Each week, physicians, allied health professionals, and students provide desperately needed health care at each of the sites, treating problems ranging from skin problems to congestive heart failure.

By reducing barriers to health care and helping these men, women, and children to achieve better health, JeffHOPE is helping them to return to mainstream society and to find housing, education, and employment.

In addition, JeffHOPE operates a patient education program in conjunction with the Greater Philadelphia Urban Affairs Coalition's job training program for the homeless, and an educational series for the Jefferson community consisting of speakers, discussion groups, plays, and movies related to issues of social responsibility and medical services for the urban underserved.

JeffHOPE is active in community and epidemiologic research, with past and current projects including an HIV and tuberculosis prevalence study; investigation into the demographic characteristics of the population the clinics serve; and research into parenting and stress among addicted women. The organization is also active in curricular issues, and last spring instituted a service/learning program in which five first- or second-year medical students are placed in community organizations for approximately 10 hours per week to assist with program development and implementation.

JeffHOPE has become a model for medical schools around the country. Health professional students and even residents volunteer at JeffHOPE because it provides them opportunities for learning and service to the community which are provided by no other part of their education. Students from other medical schools who are organizing their own homeless shelter clinic project visit to learn from JeffHOPE successes.

Student AMA Organizes Bone Marrow Drive

Gregory Gertner, Class of 2000

On the cover of a pamphlet from the National Marrow Donor Program (NMDP), a young child's eyes grab the reader's attention. Underneath the picture are the words, "I need a marrow transplant. Please Help." The Jefferson Medical College chapter of the American Medical Association is trying to help. This year, the AMA plans to conduct its first annual Bone Marrow Registration Drive. But they need your help as well.

An estimated 30,000 children and adults in the U.S. are diagnosed each year with leukemia, aplastic anemia, or any of over 60 other potentially fatal blood diseases. For many, the only hope for survival is a marrow transplant. Thirty percent of these patients will match marrow types with a family member. This means that 70 percent of marrow transplants come from unrelated donors, and the only way to become an unrelated donor is to register with the NMDP. Unfortunately, there is a significant cost to register, and, especially at the medical college level, students who may be willing to become registered with the NMDP are unable to because they simply cannot afford it. The NMDP, however, has found a corporate donor who will match any funds raised. This means that any donations from you will help twice as many students become registered with the Marrow Donor Program.

In 1995, the NMDP coordinated more than 80 transplants every month. The program could accomplish even more if its registry of volunteer donors were larger and more diverse. There may be somebody here at Jefferson who has a marrow type matching that of a dying child. This person needs your help to become registered with the NMDP. Your donation may allow a medical student to save a life now, before he or she even becomes a physician.

If you are interested in helping the AMA save lives in this way, please send correspondence to Jefferson American Medical Association, Medical Student Section, Attention: Steven Sarkisian, President, 1000 Walnut St., Apt. 2007, Philadelphia, PA 19107.

Freshman students Gregory S. Gertner, Ryan J. Zlupko, Anne M. Nelson, Kevin J. Hirokawa, Omar K. Yunis

Daniel P. Petro '2000 (right) and his sister Anastasia, a member of the Class of '99 (second from left), with their parents Paul and Mary Petro at the ***Reception for Freshman Families*** on August 21

Medical Media Services

First-year Jeannine A. Weimar-Fitzpatrick and her mother Grace Weimar

Jefferson is Reconfirmed as Delaware's Medical School

A Delaware bill signed into law in July reconfirms Jefferson's role as the medical college for the state of Delaware.

Through the Delaware Institute of Medical Education and Research (DIMER), admission to Jefferson is reserved each year for students from Delaware.

The arrangement has been in place since 1970. In lieu of funding and maintaining a medical school, the state developed "a coordinated program of premedical, medical, and graduate education among state public institutions of higher learning, Delaware hospitals, and Jefferson Medical College."

There is further give-and-take in that many Jeff students receive clinical training from Delaware physicians at the Medical Center of Delaware, the Wilmington Veterans Medical Center, or the duPont Hospital for Children, a close affiliate of Jefferson.

Jeff Physicians in the Year 2000

✔ 223 first-year students matriculated this fall at Jefferson Medical College (340 were accepted out of 11,189 applicants)

✔ 71 are female, and 152 are male

✔ eight are members of minorities

✔ 25 already hold master's degrees, and six hold doctorates

✔ 22 are part of the DIMER program for students from Delaware (see article at right)

✔ 21 are in the six-year accelerated B.S./M.D. program with Pennsylvania State University

✔ 12 are participating in the Physician Shortage Area Program which funnels graduates to practice in underserved areas

BOOKS

ALS Diagnosis

Jerry M. Belsh '75 is one of two Editors of *Amyotrophic Lateral Sclerosis: Diagnosis and Management for the Clinician,* published by Futura Publishing. 408 pages, 43 illustrations, $90. ALS is also known as Lou Gehrig's disease or motor neuron disease. Dr. Belsh is an Associate Professor of Clinical Neurology and Director of the Neuromuscular and ALS Center at UMDNJ-Robert Wood Johnson Medical School.

Changes in Care

Barry C. Dorn '67 is co-author of *Renegotiating Health Care,* published by Jossey-Bass of San Francisco. The book grew out of Dr. Dorn's teaching as Associate Director of the Program on Health Care Negotiation at the Harvard School of Public Health. He is also a Clinical Professor of Orthopaedic Surgery at Tufts University School of Medicine.

Varied Advice

Thomas D. Meade '83 of Allentown, PA is the author of *The Medical Advisor,* published by ICS Books, Merrillville, IN. It is a collection of advice about medicine collected by Dr. Meade since beginning medical school in 1979. Contributors include Jefferson alumni and faculty members.

New Clinical Text

Alvin F. Goldfarb, M.D., Professor of Obstetrics and Gynecology at Jefferson, has edited *Clinical Problems in Pediatric and Adolescent Gynecology.* Various contributors, 118 pages, illustrated. Published by Chapman and Hall, New York.

Manage Diabetes

Martin M. Mandel '47 of Blue Bell, PA has just published *Diabetes: Don't Fear It, Beat It! My Story, My Message, My Mission.* Dr. Mandel has a neurology practice based at Holy Redeemer Medical Center in Meadowbrook, PA.

High Excitement

E. Marshall Goldberg, M.D., Professor of Medicine at Jefferson, has three works of fiction available at the Thomas Jefferson University Bookstore (for contact information, see page 38 of this magazine). They are the medical thrillers *A Deadly Operation* ($14.95 paperback), *Intelligence* ($14.95 paperback), and *The Family Scalpel* ($25.00 cloth, $13.95 paperback). Published by Dufour Editions.

Alaskan Frontier

C. Earl Albrecht '32 is the subject of *Frontier Physician* by Nancy Jordan, published by Epicenter Press (Box 82368, Kenmore, WA 98028). Alaska's first full-time Commissioner of Health, Albrecht was credited with revolutionizing health care in that state. In 1963 he became a member of Jefferson's faculty as a Professor of Preventive Medicine.

An Admired Life

Carl S. Lytle '32 of Ocala, FL is the subject of *The Eternal Optimist,* written by Peg Masino, R.N. and published by Lifestyles Press. Its account of Dr. Lytle's experiences as a general practitioner includes a chapter on his medical school years at Jefferson.

Robert Neroni

The ***Raymond C. Grandon '45 Lecture*** was delivered by Mark D. Smith, M.D., M.B.A. (at right above, with David B. Nash, M.D., M.B.A., Director of Health Policy and Clinical Outcomes). Dr. Smith is Executive Vice President of the Kaiser Family Foundation, and past Executive Director of the Philadelphia Commission on AIDS.

The next Grandon Lecture will be May 15 at 8:00 A.M. in DePalma Auditorium; the speaker will be Karen Ignagni, President and CEO of the American Association of Health Plans.

New Inflammatory Bowel Disease Center is Announced

Thomas Jefferson University Hospital has established an Inflammatory Bowel Disease Center. The center's main function is the diagnosis and treatment of patients with inflammatory bowel disease (Crohn's disease, ulcerative colitis, collagenous colitis, and microscopic colitis.) Patients with uncomplicated disease will continue to be treated by their physicians. Referrals are accepted for such patients from their physicians.

The center is staffed by expert members of the Division of Gastroenterology and Hepatology and by general and colorectal surgeons with special interest and skills in dealing with inflammatory bowel diseases. Experts from radiology, pathology, and other specialties provide additional consultation.

Outstanding facilities offer up-to-date and evolving modalities for one-time evaluation, second opinions, or long-term treatment.

"Inflammatory bowel disease ranges from mild to severe to life-threatening," says Franz Goldstein '53, Professor of Medicine and acting director of the center. "There are one to two million people in the United States who suffer from bowel disease. This is a disease which requires much attention."

Dr. Goldstein has been affiliated with Jefferson for the last 40 years. He was awarded a mastership from the American College of Gastroenterology and has authored more than 130 manuscripts, many on inflammatory bowel disease. Dr. Goldstein was nominated by colleagues as one of the "best doctors in the Northeast" for inflammatory bowel disease.

The center is located on the fourth floor of Main Building.

STAFF EARN MAJOR AWARDS

John L. Abruzzo, M.D., Professor of Medicine, has been elected the first President of the Eastern Pennsylvania Osteoporosis Society.

Salman Akhtar, M.D., Professor of Psychiatry, has received three honors: Best Paper of the Year Award from the *Journal of the American Psychoanalytic Association* for his paper, "A Third Individuation: Immigration, Identity, and the Psychoanalytic Process"; the Mahler Literature Prize from the Mahler Psychiatric Research Foundation for the same paper; and the Hasenbush Memorial Visiting Professorship at Harvard Medical School.

Paul C. Brucker, M.D., President of Thomas Jefferson University, has been elected by Greater Philadelphia First to its Board of Directors. GPF is an association of business chief executives formed in 1983 with the mission of advancing economic growth and the quality of life in the Delaware Valley.

Carlo M. Croce, M.D., Chairman of Microbiology and Immunology and Director of the Kimmel Cancer Center, has been elected to the National Academy of Sciences in recognition of his achievements in research.

Larry A. Donoso, M.D., Ph.D., the Duane Professor of Ophthalmology at Jefferson and Wills Eye Hospital, has been honored by the creation of the Larry Donoso Eye Research Laboratory at Queens Medical Center, Nottingham University, in England.

Robert D. Fry, M.D., The Marks Professor and Director of Colorectal Surgery, has been appointed to the Executive Council of the American Society of Colon and Rectal Surgeons.

Alvin F. Goldfarb, M.D., Professor of Obstetrics and Gynecology, presented the Sir John Dewhurst Lecture, entitled "Adolescent Sexual Behavior: Its Impact on Future Reproduction," at the 20th annual meeting of the North American Society for Pediatric and Adolescent Gynecology.

Gerald J. Herbison, M.D., Professor and Director of Research in Rehabilitation Medicine, was honored by the American Academy of Physical Medicine and Rehabilitation as one of its 1996 Distinguished Clinician Award recipients.

Thomas B. Knudsen, Ph.D., Associate Professor of Pathology, Anatomy, and Cell Biology, has been invited to serve as a charter member of the Human Embryology and Development (2) Study Section of the National Institutes of Health.

Dennis B. Leeper, Ph.D., Professor of Radiation Oncology and Director of Radiobiology, is President-Elect and Chairman of the Program Committee of the North American Hyperthermia Society. This society supports research in the mechanisms and use of hyperthermia in the treatment of cancer.

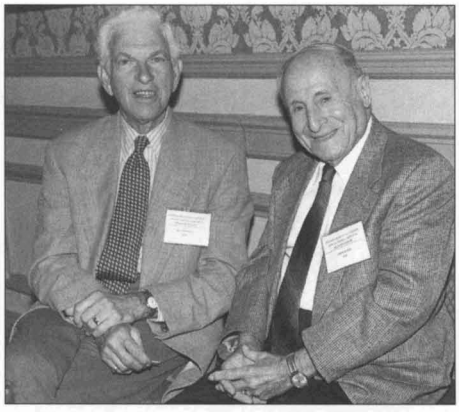
Mark Schweitzer, M.D., Associate Professor of Radiology, has won the Scholar Award of the Radiological Society of North America, an award presented to only four radiologists per year.

Troy L. Thompson II, M.D., The Lieberman Professor and Chairman of Psychiatry, has been elected to a three-year term on the national Board of Directors of Alpha Omega Alpha Honor Medical Society.

Receiving the award from Jordan J. Cohen, M.D., AAMC President (right) are (at center) Mary B. Monteith, Executive Director of the Alumni Association, and (left) Malcolm Clendenin, Associate Editor and Designer of the *Bulletin*.

125th Anniversary Celebration Wins National Award from Association of American Medical Colleges

The 125th Anniversary Celebration for the Jefferson Medical College Alumni Association has won a national prize from the Association of American Medical Colleges. The AAMC's Award for Excellence in Public Affairs was presented to Jefferson for this multifaceted celebration of the history and future of the medical college. It included four issues of the *Bulletin* culminating in the special Spring 1995 issue, a video, a Mayor's proclamation, and enhanced events during 1995 with a special scientific symposium and gala Reunion Weekend. The project's success was a collaboration of the leadership of the Alumni Association and the professional talents of the Jefferson Medical College Alumni Office. Among the judges' comments: "Much to celebrate and you did it so well." "The magazine could not have been better."



At the ***Dinner for Class Agents and Reunion Chairmen*** on September 30 are (above) John T. Comber '91, Lina P. Sinha '91, and Benjamin Bacharach '56, Chairman of the President's Club.

(At left) L. Roy Newman '49 and Leon L. Berns '30

Don Walker

Eugene F. Bonacci '56 and Sharon B. Mass '93 at the Class Agents Dinner September 30

John R. Prehatny '57 with Herbert G. Hopwood Jr. '58

The reception in the Rotunda

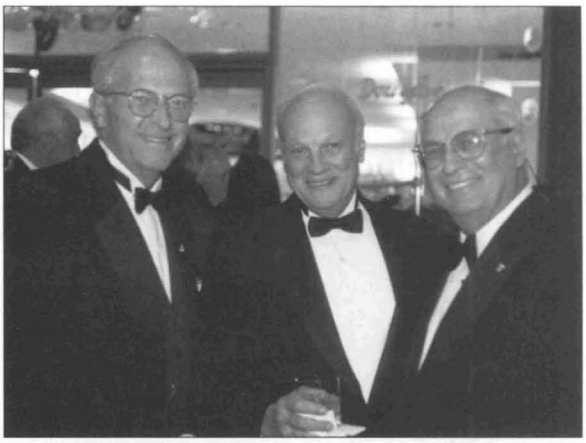
Sidney Kimmel Receives Cornerstone Award at President's Club Dinner

Sidney Kimmel was honored with the Cornerstone Award at the President's Club Dinner on October 4.

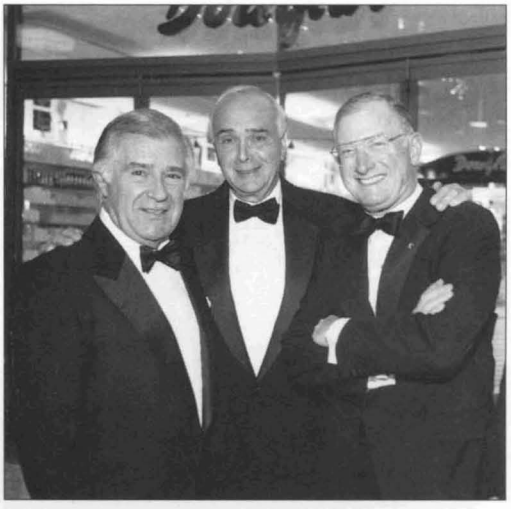
In appreciation of a gift of $10 million from the Sidney Kimmel Foundation, Jefferson's cancer center was named the Kimmel Cancer Center earlier this year (see the June *Bulletin*). Mr. Kimmel is founder and chairman of the Jones Apparel Group and a longtime supporter of medical interests.

The President's Club Dinner was held at the Ritz-Carlton and adjoining Rotunda at Liberty Place, the smart Center City complex of glass, blue metal, and granite designed by Helmut Jahn. Receiving special recognition at the dinner were 16 new members of the Winged Ox Society and four new Fellows of the President's Club.

Robert Neroni



Herbert E. Cohn '55; Francis E. Rosato, M.D. (the Gross Professor and Chairman of Surgery); and Melvin L. Moses '62



Emanuel Rubin, M.D. the Aponte Professor and Chairman of Pathology, Anatomy, and Cell Biology, and Robert L. Brent, M.D., Ph.D., the Distinguished Professor and past Chairman of Pediatric

Sidney Kimmel with David L. Paskin '64 and Richard H. Rothman ORS'68

University President Paul C. Brucker, M.D.; Sidney Kimmel (holding the miniature statue of Thomas Jefferson which was presented to him); Rena Rowan; Carlo M. Croce, M.D., Director of the Kimmel Cancer Center of Thomas Jefferson University; and Joseph S. Gonnella, M.D., Dean and Senior Vice President for Academic Affairs

Dean and Senior Vice President for Academic Affairs Joseph S. Gonnella, M.D. and Kay Huebner, Ph.D., Professor of Microbiology and Immunology

OBITUARIES

Correction: The obituary in the June 1996 *Bulletin* of ***Benjamin Provisor '32*** did not state that he is survived by his wife, Lenore, of Passaic, NJ, and two daughters. Dr. Provisor had practiced in Passaic, after having taken his postgraduate training in surgery at the University of Pennsylvania. Dr. Provisor's grandson, Eric P. Kleinbaum, is currently a first-year student at Jefferson Medical College.

Louis F. Burkley Jr. '20 died June 16, 1996 at age 99 years. He practiced obstetrics in Easton, PA and served on the obstetrical staff of Easton Hospital, Easton, PA. He co-founded the hospital's prenatal clinic and taught obstetrics at the hospital's nursing school for 35 years. He earned the nickname "Papa" Burkley because of his compassionate devotion to patients. He is survived by a daughter.

Verne S. Caviness '21 died August 22, 1996 at age 101 years. He opened the first internal medicine practice with a special interest in cardiovascular diseases in Raleigh, NC in 1923. He served as Chief of General Medicine at St. Agnes Hospital and Chief of Cardiovascular Medicine at Rex Hospital, Raleigh, NC, and was a Fellow of the American College of Physicians. He did pioneering research with insulin and on hypertension and was listed in *American Men of Science*. He was an Associate Professor of Clinical Medicine at the University of North Carolina School of Medicine, Chapel Hill, NC. In 1985 he established the Dr. Verne S. Caviness Professorship of Investigative Medicine at that medical school. In 1991 the school's Clinical Research Unit was renamed and dedicated the Verne S. Caviness General Clinical Research Center. He is survived by a son and two daughters.

Bruce A. Grove '26 died February 10, 1996 at age 95 years. He practiced in York, PA. He served as Head of the Department of Ophthalmology at York Hospital, York, PA for 25 years. He was a Fellow of the American College of Surgeons and the American Academy of Ophthalmology and a past President of the York County Medical Society. He is survived by two sons.

Reginald A. Allen '32 died August 3, 1996. He practiced pediatrics in Providence, RI for 53 years, retiring in 1988. He was a member of the New England Pediatric Society and a Fellow of the American Academy of Pediatrics. He is survived by his wife, Annette, two sons and two daughters.

George A. Baver '32 died April 8, 1996. He lived in Pennsburg, PA and had practiced family medicine. He is survived by his wife.

John Bower '33 died October 14, 1996. A member of Alpha Omega Alpha Honorary Fraternity, he practiced psychiatry in Reading, PA. He was Director of the Department of Psychiatry and Neurology at Reading Hospital and a Staff Psychiatrist at St. Joseph's Hospital, Reading. PA. He is survived by three sons. Son John is Jefferson '66 and son Edward is Jefferson '70.

Gilbert M. Halpern '34 died July 15, 1996. He practiced general and occupational medicine in Honolulu, HI and was on staff at Queens Hospital in Honolulu. He was Medical Director of the Dole Company, Honolulu, HI for 35 years. He is survived by several children.

Benjamin P. Houser '34 died May 18, 1996. He practiced as an eye, ear, nose and throat specialist in Tamaqua, PA. He was on staff at the former Coaldale State General Hospital, Coaldale, PA, Gnaden Huetten Memorial Hospital, Lehighton, PA and Pottsville Hospital, Pottsville, PA. He is survived by his wife, Ruth, a son and two daughters.

Dermot Lohr '34 died June 28, 1996. He practiced public health in Lexington, NC. He was associated with the Smith-Lohr Clinic and Lexington Memorial Hospital, Lexington, NC. He is survived by his wife, Blanche, and two sons.

Joseph F. Hughes '35 died September 1, 1996. A board-certified General Surgeon and Fellow of the American College of Surgeons, he was Chief of Surgery at Wilmington Medical Center and St. Francis Hospital, Wilmington, DE. After retiring in 1979, he moved to Honolulu, HI and worked as Medical Officer, disability evaluation, Veterans Administration Regional Office, Honolulu, HI. He is survived by his wife, Mary, two sons, and a daughter.

Frank M. Grem '40 died July 21, 1996. A board-certified Anesthesiologist, he practiced at Oak Park Hospital, Oak Park, IL. He held appointments as Assistant Professor of Anesthesiology, University of Illinois School of Medicine and Professor of Anesthesiology, Loyola University School of Dentistry. He served as President, Chicago Society of Anesthesiologists in 1950 and President, Illinois Society of Anesthesiologists in 1959. He is survived by three daughters and a son. Son Philip is Jefferson '76 and daughter Jean is Jefferson '80.

Dale T. Anstine '42 died October 15, 1996. He was an internist with a subspecialty of cardiology and practiced in Hollywood, FL. He was a past Chief of Staff at Doctors' Hospital of Hollywood, and a Fellow of the American College of Cardiology. He is survived by his wife, Mabel, two sons, and two daughters.

Richard D. Bausch '42 died July 19, 1996. He practiced in Allentown, PA and was a Fellow of the American Academy of Family Physicians. He was on staff at Sacred Heart Hospital, Allentown, PA. He is survived by his wife, Emma, four sons, two daughters, a stepson, and a stepdaughter.

John W. Galson '42 died August 9, 1996. He practiced internal medicine in Philadelphia, PA and was on staff at Presbyterian Hospital, Philadelphia, PA. He is survived by his wife, Margaret, a son, and two daughters.

Stephen J. Marthouse '42 died September 6, 1996. He maintained a general practice in Lewistown, PA for 35 years. He is survived by his wife, Harriette, three sons, and two daughters.

Stanley N. Clark S'44 died May 9, 1996 in Provo, UT, it has been ascertained.

David A. Culp S'44 died October 7, 1996. A board-certified urologist, he was Professor and Chairman of the Department of Urology, University of Iowa College of Medicine, Iowa City. He contributed many articles to the urologic literature and co-authored three books. A Fellow of the American Urologic Association, he later served as President of the organization. He is survived by his wife, Anna, three sons and two daughters.

Stephen Sorokanich S'44 died April 27, 1996. He was a General Practitioner in Old Forge, PA. He is survived by his wife and son, Stephen Jr., who is Jefferson '81.

Oram R. Kline Jr. '45 died September 11, 1996. A board-certified Ophthalmologist, he held staff appointments at Cooper Hospital, Camden, NJ, Underwood Hospital, Woodbury, NJ, and Wills Eye Hospital, Philadelphia, PA. He held a Jefferson faculty

appointment as Clinical Professor of Ophthalmology and served as President, New Jersey Ophthalmologic Society in 1970. He is survived by his wife, Sue Ann, a son, and a daughter.

Rocco P. Sciubba Jr. '45 died August 1, 1996. He was in general practice in Broomall, PA and held a staff appointment at Haverford-Mercy Hospital, Ardmore, PA. He is survived by his wife, Jeanne, two sons and two daughters.

I. Ralph Burbridge Jr. '46 died August 19, 1996. Certified by the American Board of Psychiatry and Neurology, he practiced in Erie, PA. He held a staff appointment at Hamot Medical Center, Erie, PA and a teaching appointment at Western Psychiatric Institute, Pittsburgh, PA. He is survived by his wife, Olga, four daughters, and son Geoffrey, Jefferson '77.

Edwin M. Mszanowski '47 died August 14, 1996. A General Surgeon, he practiced in Erie, PA. He was a full time member of the active surgical staff at Hamot Medical Center, Erie, PA. He is survived by his wife, Millie, two sons, and three daughters.

Charles R. Barton Jr. '48 died November 3, 1996. He was in general practice in Glenolden, PA and served as borough Health Officer. He relocated to Scottsville, VA in 1970 and practiced as a Country Doctor until retirement in 1981. He is survived by his wife, Marjorie, and four sons.

Charles G. Steinmetz III '48 died September 16, 1996. A board-certified ophthalmologist, he was on staff at Bryn Mawr Hospital, Bryn Mawr, PA and Wills Eye Hospital, Philadelphia, PA where he had served as Chief of the General Ophthalmologic Service. He was a Clinical Associate Professor of Ophthalmology, Jefferson Medical College. He is survived by his wife, Megan, a son, a daughter, and two stepdaughters.

Robert L. Evans '52 died October 22, 1996. A board-certified internist, he had a distinguished career in medical education, including teaching appointments at Jefferson Medical College and the University of Maryland. He was the first Director of Medical Education at York Hospital, York, PA and, in 1995, the Education Building at York Hospital was named in his honor. He later served as the founding Dean of the University of Illinois School of Medicine, Rockford, IL, and as President of the Cooper Medical Center, Camden, NJ. A member of numerous medical and educational organizations, he was President of the Association for Hospital Medical Education. He served as an Alumni Trustee on the Board of Trustees of Thomas Jefferson University, 1971–1977. He is survived by his wife, Peggy, and two sons.

Louis J. Wagner '52 died September 28, 1996. A board-certified general and thoracic surgeon, he practiced in Oil City, PA. He was on staff at the Franklin Regional Medical Center, Franklin, PA. He is survived by his wife, Mary, and a daughter.

Robert N. Cottone '56 died July 21, 1996. A board-certified Urologist, he practiced in Trenton, NJ. He was on staff at St. Francis Medical Center, Trenton, NJ where he was Chief of Urology and a former President of the Medical Staff. He is survived by his wife, Jackie, five sons, and two daughters.

Howard S. Silverman '83 died August 21, 1996. A noted researcher and clinician, he was an NIH-funded cellular physiologist and an Assistant Professor of Medicine, Johns Hopkins University School of Medicine, Baltimore, MD. He is survived by his wife, Roseanne, and two sons.

Harold L. Israel '34

A noted pulmonary disease researcher and clinician and an Emeritus Professor of Medicine at Jefferson, Harold L. Israel '34 died November 22, 1996. His major clinical interest was sarcoidosis and his work on this disease received international recognition. He had been a member of the International Committee on Sarcoidosis since 1958 and was Vice President of the 10th International Conference on Sarcoidosis in 1984. A familiar figure on the Jefferson campus, Dr. Israel held many important positions during his career including Assistant Director, Tuberculosis Division, Philadelphia Department of Health; Assistant Visiting Physician and Visiting Physician, Philadelphia General Hospital; Pulmonary Consultant, Valley Forge Army Hospital, Philadelphia Naval Hospital, and Wilmington Veterans Administration Hospital; Member, National Heart and Lung Institute Task Force on Research Approaches to Respiratory Diseases; and, since 1976, an Honorary Member, British Thoracic Society.

Following a two-year internship at Philadelphia General Hospital, he pursued his interest in pulmonary diseases at the Henry Phipps Institute, University of Pennsylvania and earned an M.P.H. degree from the University of Pennsylvania in 1942. He spent three years in the U.S Army Medical Corps during World War II, attaining the rank of major. Following teaching appointments at the University of Pennsylvania, Woman's Medical College and the Graduate School of Medicine, University of Pennsylvania, he returned to Jefferson in 1959 as Clinical Professor of Medicine. He was made Professor of Medicine in 1972. On his retirement in 1982, he was made Emeritus Professor and was awarded the Dean's Medal in recognition of his many contributions to medical education, clinical care, and innovative research. Over his career Dr. Israel published 201 scientific articles. He is survived by two sons, two daughters, and two stepsons. Son Daniel is Jefferson '67.

Gustave Edward Zerne OTO '53 died July 12, 1996. He received his postgraduate education in otolaryngology at Jefferson and practiced in Lebanon, PA.

J. Leonard Ivins P'66 died October 20, 1996. He completed a psychiatry residency at Jefferson. He was on staff at Haverford State and Haverford-Mercy Hospitals, Haverford, PA, and Belmont Hospital and the Institute of Pennsylvania Hospital, Philadelphia, PA. He is survived by a son and two daughters.

Margaret Riley Scimeca P'78 completed a psychiatric residency at Jefferson. She died on an unknown date in 1996, it has been ascertained. She is survived by her physician husband.

Jole C. McCurdy P'81 completed a psychiatric residency at Jefferson. He died on an unknown date in 1991, it has been ascertained.

Suzanne M. Wester OBG'88 completed a residency in obstetrics-gynecology at Jefferson. She died January 9, 1996, it has been ascertained.

Gartland Elected Alumni Trustee

John J. Gartland S'44 was elected an Alumni Trustee this year through the ballot that was mailed to each Jefferson graduate, including postgraduate alumni.

The James Edwards Professor Emeritus of Orthopaedic Surgery at Jefferson Medical College, Dr. Gartland headed the department from 1970 to 1985. He is the author of *Fundamentals of Orthopaedics,* a past President of the American Academy of Orthopaedic Surgeons, and a former Associate Editor of the *Journal of Bone and Joint Surgery.*

Miller Receives ASME's Holley Medal

Bernard J. Miller '43 received the prestigious Holley Medal on November 20 at the annual international meeting of the American Society of Mechanical Engineers (ASME) in Atlanta. This award was established in 1924 to honor Alexander Lyman Holley. It was given this year to Dr. Miller for the innovative application of fluid mechanics in the design of a feedback control system enabling the heart-lung machine to assist with an open-heart operation performed for the first time on a human being in May 1953.

Dr. Miller was the research associate of John H. Gibbon Jr. '27 from 1950 to 1953, and through his collaboration, the heart-lung machine developed the necessary controls and fluid mechanics and feedback control systems to enable the first successful open-heart operation in the world.

In addition to this important work, Dr. Miller has carried out research on the further design and development of heart-lung machines; and the use of extracorporeal circuits for the treatment of malignant tumors of the extremities with high-dose cancericidal agents, while the circulation of the extremity is isolated during treatment by an extracorporeal circuit and the escape of drug to the general circulation is minimized.

Dr. Miller has taught anatomy at Jefferson for more than 40 years as a full Professor and currently is an Honorary Associate Professor in the surgical department. He received an honorary degree of Doctor of Science from Villanova University in 1982. Three of his five children, as well as his son-in-law, are Jefferson graduates.

'32 65th Reunion June 6–8

Nathan S. Schlezinger of Wyncote, PA was on stage at the Academy of Music at Commencement last June when his grandson, Jeffrey A. Simon, M.D., graduated in the Class of '96. Dr. Schlezinger is an Emeritus Professor of Neurology.

'42 55th Reunion June 6–8

J. Arthur Steitz of Medford, NJ has retired and is "enjoying being in a retirement community."

'46

David G. Simons of Huntington Beach, CA is completing his second generous U.S. Scientist Award from the Alexander von Humboldt Foundation. As a result of his collaboration with Professor Siegfried Mense at the University of Heidelberg, Dr. Simons submitted a paper with Professor Mense that received a competitive award from the Strathmann company, the Forderpreis Muskelrelaxation (competitive award for the best paper on the subject of muscle relaxation).

'47 50th Reunion June 6–8

James T. Helsper of Pasadena, CA has been appointed Professor of Clinical Surgery

Please submit news for Class Notes to:
Attention: *Alumni Bulletin*
Jefferson Medical College of Thomas Jefferson University
1020 Locust Street, Suite M-41
Philadelphia, PA 19107-6799

Would you like to contact the Alumni Office electronically?
If so, you can send your name, class year/specialty, and information such as address changes or personal and professional changes to: *jmcalums@jeflin.tju.edu.* The e-mail address of the *Bulletin* is: *iedl72w@tjuvm.tju.edu.*

❧

Readers are encouraged to submit nominations for:
1) ***Alumni Trustee of Thomas Jefferson University:*** One is elected each year for a three-year term (he or she may be reelected for one additional term). Please submit names of worthy candidates to "Attention: Alumni Trustee Committee," 1020 Locust Street, Suite M-41, Philadelphia, PA 19107.
2) ***Alumni Achievement Award:*** Although the award carries no monetary stipend, each recipient's name is permanently affixed to a plaque prominently displayed at the entrance to Jefferson Alumni Hall. The recipient is presented with a handsome silver tray, suitably engraved and bearing the seal of the medical college, as the highlight of the Alumni Banquet each June. The Achievement Award Committee of the Alumni Association is charged with the final selection; the committee's decisions are not subject to review. Please direct curricula vitae and bibliographies of alumni whose professional activities are sufficiently outstanding to warrant consideration to "Attention: Achievement Award Committee," 1020 Locust Street, Suite M-41, Philadelphia, PA 19107.

(full-time faculty) at the University of Southern California School of Medicine in Los Angeles.

'48

Eugene P. Hughes of Plymouth Meeting, PA has retired and is doing much golfing, hunting, and fishing. His wife, Jane, has accepted a position as President of Whitemarsh Valley Country Club.

'49

The Albert Einstein Society honored ***L. Roy Newman*** of Elkins Park, PA at its annual dinner on September 25, 1996. Dr. Newman was recognized for his service to Albert Einstein Medical Center and the Einstein Society that supports medical research and innovative patient care.

'52

James E. Clark of Swarthmore, PA was honored in November by Crozer-Chester Medical Center. The occasion was the National Philanthropy Day luncheon organized by the Greater Philadelphia Chapter of the National Society of Fund Raising Executives. Dr. Clark chaired Crozer-Chester's Medical and Dental Staff Capital Campaign, which raised over $2.1 million for an Education Center and Ambulatory Care Pavilion. The center is named in his honor. Dr. Clark is Chairman of the Department of Medicine and Director of Medical Education at Crozer-Chester, and a member of the Board of Directors of the Crozer-Keystone Health Systems. In past years at the National Philanthropy Day luncheon, ***J. Wallace Davis '42*** and ***Benjamin Bacharach '56*** have been honored by Jefferson Medical College.

'54

Robert A. Hinrichs of Corona Del Mar, CA has limited his practice to two to three days a week, "so now my golf is better."

'55

Joseph A. Heaney of Cumberland, WI is a locum tenens psychiatrist specializing in forensic psychiatry for the state mental health system. His wife, Mary Brust Heaney, has published a book, *Beloved Stranger: Reflections on Mental Illness,* drawing on their years in psychiatry.

J. Donald Schultz is happily retired in Shelburne, VT along with ***Robert W. Lukens Jr.***

'57 40th Reunion June 6–8

George A. Salverian of Huntingdon Valley, PA has recently retired, with 43 years of devoted dedication following his excellent training at Jefferson. His wife, Ilah, and family joined him in celebrating his retirement.

'58

Edwin R. Concors of Rydal, PA is still active in practice.

John K. Kreider of Manheim, PA is enjoying taking care of prisoners at Dauphin County and Berks County State Hospitals, and is enjoying his five wonderful grandchildren.

'60

William H. Mahood of Flourtown, PA was elected an AMA Trustee in June 1996.

Rudolf Bee of New Britain, CT is still practicing general ophthalmology. He has three children, ages nine to 12. Recently, he received the highest license in amateur radio.

'61

Arthur N. Meyer of Kingston, PA is in private practice of hematology/oncology in Kingston. His wife, Barbara, is his office manager.

William B. Pratt of Gallup, NM has been at the Gallup Indian Medical Center as an orthopaedic surgeon since 1987. His plan is to retire in "about two years."

'63

John N. Rightmyer of Hamburg, PA has retired from his family practice and from his work at Wernersville State Hospital. Dr. Rightmyer will be the District Governor for District 7430 Rotary International from July 1997 through 1998.

'66

Franklyn R. Cook of Carmichael, PA is feeling excellent despite a past pneumonectomy for lung cancer.

Michael P. Dolan of New Orleans, LA has now retired as the Medical Director of Health Services of Lockheed Martin Manned Space Systems. He and his family plan to remain in New Orleans. Now they have the time to go sailing in the Caribbean!

'67 30th Reunion June 6–8

Carl L. Stanitski of Grosse Pointe Farms, MI is now on

Bowman is First Chair of Family Medicine at Penn

Marjorie A. W. Bowman '76 has been appointed the first Chairman of the newly created Department of Family Practice and Community Medicine at the University of Pennsylvania School of Medicine. Dr. Bowman is a past President of the Society of Teachers of Family Medicine and is President-Elect of the North Carolina Academy of Family Physicians (until her appointment at Penn she chaired the Department of Family and Community Medicine at Bowman Gray School of Medicine of Wake Forest University).

"I've been involved for a long time in growing family medicine at academic institutions," she says. "I'm pleased to have the hands-on opportunity to do this at Penn."

Dr. Bowman is Editor of the *Archives of Family Medicine* and serves on the editorial board of the *Journal of the American Medical Association*. She has been elected to the Institute of Medicine of the National Academy of Sciences.

the Editorial Board of the *Journal of Pediatric Orthopaedics*. He was also just named Chairman of the Education Committee of the Scoliosis Research Society, succeeding ***Peter D. Pizzutillo '70*** of Wynnewood, PA.

Matthew White of Gig Harbor, WA has expanded his family medicine practice with two new partners.

'69

Richard Gross of Granite Bay, CA passed the CAQ (Certificate of Added Qualifications) Boards in Interventional Radiology (Vascular Radiology) in November 1995.

'70

Larry S. Cohen of North Miami, FL is now the Medical Director of Williams Island Medical Group. Larry and his wife, Rona, celebrated their 25th wedding anniversary on June 20.

Neil O. Thompson of Baltimore, MD returns to Thailand in December 1996.

'71

Christopher K. Balkany of St. Cloud, MN has become board-certified in endocrinology and metabolism.

Joseph L. Seltzer of Rosemont, PA has been elected President of the Society of Academic Anesthesia Chairs for a two-year term.

'72 25th Reunion June 6–8

Steven A. Ager of Cherry Hill, NJ was voted by New Jersey physicians to be one of the psychiatrists by whom they themselves would most want to be treated, in a poll conducted by *New Jersey Monthly* and released in its April 1996 Top Docs issue.

'73

Paul A. Bialas of Warren, PA continues in active general internal medicine practice in Warren, PA. He serves as Vice President of the Medical Staff and is a member of the Board of Trustees at Warren General Hospital. Governor Ridge has just appointed Dr. Bialas to a five-year term on the Warren State (Psychiatric) Hospital to commence in January 1997.

Leland D. Cropper Jr. of Oilville, VA has a private practice of vascular and interventional radiology and diagnostic radiology. He is now Chief of Radiology at Healthsouth Medical Center in Richmond, VA.

Joanna R. Johnson of Malvern, PA married David Johnson Jr. on October 8, 1995. Congratulations!

Richard M. Sostowski of Livingston, NJ recently passed the subspecialty boards in forensic psychiatry.

'74

William A. DiCuccio of Butler, PA is the Medical Director for Sunnyview (Butler County's nursing home) and Butler County Prison.

Dr. Ashley-Gilbert

'76

Ann Ashley-Gilbert and ***Genester Wilson King '82,*** both of Altamonte Springs, FL, along with Billie Jean Pace, M.D., have formed "the first women's group gynecology practice in Seminole and Lake Counties" in Florida. The Altamonte Women's Center opened in September 1996.

Dr. King

Melissa R. Spevak of Baltimore, MD and her husband, Phil, are both working at Johns Hopkins Hospital, she in pediatric radiology and he in pediatric cardiology. They are enjoying their children Sarah, age four, and James, age 21 months.

'77 20th Reunion June 6–8

Dale N. Goode of Yardley, PA is practicing emergency medicine in Trenton, NJ and also enjoying occupational medicine at Lockheed-Martin. He went to Russia and Kazakhstan in May.

'78

Bruce E. Nayowith of Rhinebeck, NY is working in a small emergency room in the Catskills, and helping his wife school their four children at home.

Statement of Ownership, Management, and Circulation (PS Form 3526)
(required by 39 U.S.C. 3685, United States Postal Service)

1. Publication title: *Jefferson Medical College Alumni Bulletin*
2. Publication number: 00215821
3. Date of filing: 10/96
4. Issue frequency: four per year
5. Number of issues published annually: four
7. Complete mailing address of office of publication: Suite M-41, 1020 Locust Street, Philadelphia, PA 19107
8. Mailing address of general business office of publisher: same as above
9. Publisher: Jefferson Medical College of Thomas Jefferson University (address above)
   Editor: Mary B. Monteith (address above)
   Managing Editor: Malcolm Clendenin (address above)
10. Owner: Jefferson Medical College of Thomas Jefferson University (address above)
11. Bondholders, mortgagees, and other security holders owning or holding one percent or more of total amount of bonds, mortgages, or other securities: none
12. For nonprofit organizations authorized to mail at special rates: the purpose, function, and nonprofit status of the organization, and the exempt status for Federal income tax purposes have not changed during the preceding 12 months

15. Extent and nature of circulation	Average Number Copies of Each Issue During Preceding 12 Months	Actual Number Copies of Single Issue Published Nearest to Filing Date
A. Total number of copies (net press run)	18,500	18,500
B. Paid and/or requested circulation		
1. Sales through dealers, carriers, street vendors, counter sales	0	0
2. Paid and/or requested mail subscriptions	17,900	17,900
C. Total paid and/or requested circulation	17,900	17,900
D. Free distribution by mail	290	290
E. Free distribution outside the mail	300	300
G. Total distribution	18,490	18,490
H. Copies not distributed	10	10
I. TOTAL	18,500	18,500
Percent paid and/or requested circulation	97%	97%

Scott M. Goldman '76 of Philadelphia (third from left, above) was the special honoree November 21 at the testimonial dinner of the Main Line Division of the American Heart Association of Southeastern Pennsylvania. He's one of the youngest individuals to be honored in this way. With him in this photo are Lawrence Frame, M.D., President of the AHA of Southeastern Pennsylvania; Harmon Spolan, President of Jefferson Bank; and Peter Kowey, M.D., Chief of Cardiovascular Diseases at The Lankenau Hospital (a member of the Jefferson Health System).

Neil H. Shusterman of Wynnewood, PA is enjoying pharmaceutical medicine at SmithKline Beecham. Dr. Shusterman is in charge of worldwide development of cardiovascular and renal drugs.

'79

Thomas J. Marshall Jr. of Arlington, TX was recently appointed Director of Surgery and Surgical Subspecialties for Kaiser Permanente, Southwest Division, based in Dallas.

Brian R. Ott of Barrington, RI was promoted to Associate Professor in the Department of Clinical Neurosciences at Brown University School of Medicine.

'80

Stephen A. Geraci of Germantown, TN is Associate Program Director, Medicine and Cardiology at the University of Tennessee and Assistant Chief of Medicine at the Veterans Administration Medical Center in Memphis.

'82 15th Reunion June 6–8

Christine C. Gamburg of Berwyn, PA is in a clinical anesthesia practice at Delaware County Community Hospital. She is also the Director of Drexel Anesthesia Pain Clinic.

'83

Lauren E. Bickel of Owensboro, KY has delivered a baby boy. John Timothy Bickel was born on July 20. Timmy joins Emily, who turns three in January. While Dr. Bickel is enjoying her full-time motherhood, she also has a part-time family practice. May we say, "You go girl!"

Timothy M. Heilmann of Williamsport, PA is an Associate Director of the Williamsport Hospital Family Practice Residency. His family now include his wife, Susie, and their six children, Katie, Becky, Michael, Caroline, Elizabeth, and Andrew.

Thomas D. Meade and ***Charles Norelli,*** both of Allentown, PA, set a Masters' World Record in swimming this year in the 200-meter freestyle relay. Dr. Norelli won six individual events and one second place at the U.S. Masters Swimming National Championships in Cupertino, CA. Also this past year, Drs. Meade and Norelli, who train together, broke another world record, in a four-man team event.

Dr. Meade presented his research on "Femoral Nerve Block Allowing Predictable Outpatient ACL Surgery" at the North American Arthroscopy Association meeting in Washington, DC. He was also selected as an orthopaedic consultant for the Philadelphia Eagles summer camp at Lehigh University.

Gary Y. Ott of Cincinnati, OH has accepted a position as Associate Professor of Surgery, Division of Cardiothoracic Surgery at the University of Cincinnati Medical Center. He also assumes duties as Director of Thoracic Transplantation. He would love to hear from any classmates in the area.

Andrew B. Sattel of Moorestown, NJ recently became a member of the American Society for Surgery of the Hand and a Fellow of the American College of Surgeons.

'84

Louis A. Kazal Jr. of Ganado, AZ is still on the Navaho Reservation in Arizona. He has been appointed Medical Director of Sage Memorial Hospital and promoted to Clinical Associate Professor of Family Medicine at Baylor College of Medicine.

'85

Harry A. Cooperman of Voorhees, NJ is serving as President of the Medical Staff at Our Lady of Lourdes Medical Center, Camden, NJ. He is a diagnostic radiologist with Lourdes Radiology Associates in Camden County, NJ.

Carol Boerner '76 of Boston with her two six-month-olds (llamas, that is): Kismet and Mozart. Dr. Boerner enjoys getting away to her llama farm in Vermont.

Ralph J. LaNeve of Brentwood, TN is now practicing at Columbia Summit Medical Center in Nashville, TN. Ralph and his wife, Carol, have two children, David, age seven, and Brynna, three. The LaNeve family miss our Philly cheesesteaks (though they *can* now buy Tastykakes).

'86

Robert L. Robles of San Francisco is an Assistant Clinical Professor in the Department of Medicine at San Francisco General Hospital. He practices hematology, oncology, and AIDS care.

'87 10th Reunion June 6–8

William E. Burak Jr. of Columbus, OH has been appointed an Assistant Professor of Surgery in the Division of Surgical Oncology at the Ohio State University and Arthur G. James Cancer Hospital and Research Institute. He and his wife, Susan, just had an addition to the family. Alexandra Adela was born July 15, 1996. Ryan Stephen, their son, turned four in October.

Caesar A. DeLeo III of Evanston, IL is now Associate Medical Director at CIGNA Health Care of Illinois.

John F. and ***Deanna Wilson*** are proud to announce the birth of their daughter, Elizabeth Kirby Shaw Wilson, born July 22. Elizabeth joins brothers John, age 11, Ritchie, 10, and sisters Caroline, seven, and Alexandra, five.

'88

Gregory E. Herman of West Point, NY is in charge of the primary care clinic at Keller Army Hospital. He's been a family doctor now for the past eight years and plans on "hanging it up in two years or so." Meg, his wife, works part-time in an early intervention program visiting children with possible developmental delays. The Hermans have four children: Katie, who is six; Sara, four; Erin, two; and Adam, eight months. The family hope to move back to Philadelphia soon.

Jean M. Nelson of Pfafftown, NC has been promoted to Assistant Professor of Anesthesia at Bowman Gray School of Medicine in Winston-Salem, NC. She had been an Instructor in Anesthesia since 1992.

John T. Rich Jr. of Clarks Summit, PA has joined an orthopaedic practice in Scranton, PA after finishing a hand surgery fellowship at Allegheny General Hospital in Pittsburgh.

Craig G. Richman of Erie, PA and his wife, Linda, are the proud parents of Stefanie, age three, and Eric, two. Craig is President of the Erie County Medical Society and President of a 10-physician group, Presque Isle Psychiatric Associates.

Suzanne T. Sundheim of Boulder, CO is the proud mother of Cole Scott Voeller Sundheim, born October 10. Suzanne is also Co-Director of Consultative Mental Health Services to Persons with Developmental Disabilities, in Programs for Public Psychiatry, and Assistant Professor of Psychiatry at the University of Colorado.

Kevin M. Zakrzewski of Horsham, PA has received an appointment as Vice President of Medical Affairs at Graduate Hospital in Philadelphia.

'89

Nick Maravich Jr. of Isle of Palms, SC proudly announces the birth of his second daughter, Brianna Brooke, born July 24. Nick also has been appointed Head of the Radiology Department at the Naval Hospital in Charleston, SC. He has completed a novel, *Fingers Uncrossed,* which is awaiting publication.

Philip S. Schwartz of Landstuhl, Germany has completed his fellowship in rheumatology and started a two-year tour as a rheumatologist.

Andrew P. Sirotnak of Denver, CO has been appointed Director of the Child Advocacy and Protection Team at the Children's Hospital in Denver. He is also Assistant Professor of Pediatrics at the University of Colorado School of Medicine. He is active in the Denver Chapter of the American Academy of Pediatrics, and is a board member of the Colorado Professional Society on the Abuse of Children (COPSAC). He is a founding member of the newly formed Denver County Child Fatality Review Committee.

Charles D. Tullius of Savannah, GA is now practicing obstetric anesthesia at Chandler Hospital. He is pleased to note that ***Kyrin Dunston '92*** and ***Rebecca Hogue '90*** are also in Savannah. From time to time, Dr. Tullius will do anesthesia work for ***Richard Greco '83*** at his plastic surgery center. Charles has two children, David, age two and one-half, and Claire, age six months.

Prodromos Ververeli of Allentown, PA is celebrating the birth of his son, Alexander Robert, born March 21, 1996. His daughter, Elizabeth, turned three years old in June.

Madeline S. Wood-Cicchinelli of West Chester, PA and her husband have one child, Carissa Claire, who turns three in December.

'90

Alice R. Dick of Los Angeles, CA is now a staff internist at the Medical Group of Beverly Hills, Inc., a division of the Cedars-Sinai Healthcare Foundation.

Marc J. Levine of St. Petersburg, FL has joined Tampa Bay Orthopaedic Specialists with offices in St. Petersburg. The group has provided adult orthopaedics in that area for 25 years. Dr. Levin completed his spine surgery fellowship at Emory University Hospital last July. He is now a dad as well as happily married to Robine. Benjamin Nathan Levine celebrates his first birthday in January.

Your diploma is from Jefferson Medical College of Thomas Jefferson University—please refer to your degree in this way.

'91

Andrea E. Gordon of Federal Way, WA completed a two-year fellowship in Family Practice Faculty Development in Pittsburgh, PA through a project sponsored by St. Margaret Memorial Hospital. While completing her fellowship, she'd done a research project in a complementary medicine modality called Therapeutic Touch, which is currently being prepared for submission to a journal. Andrea has started her new faculty position in the rural branch of the Tacoma Family Practice Residency Program in Puyallup, WA.

'92 Fifth Reunion June 6–8

Kyrin Dunston has joined Chatham Ob-Gyn Associates in Savannah, GA. She received the Resident Achievement Award from the Society of Laparo-Endoscopic Surgeons while a resident at the Medical Center of Delaware.

Stephen B. Kupferberg and ***Marcia Liu*** of Martinez, GA are the proud parents of Jacob Eric Kupferberg, now one-and-a-half. They are at the Medical College of Georgia where Stephen is completing the last year of his otolaryngology residency, and Marcia is in the second year of her cardiology fellowship.

Maria E. Pharr of Havertown, PA has received a Jefferson faculty appointment as an Assistant Professor of Family Medicine.

Helen K. Sava of Honolulu, HI is the proud mother of Vincent James Sava III, born February 28, 1996. Dr. Sava is an attending physician at the Tripler Army Medical Center Family Practice Residency Program.

Congratulations to ***C. Anthony Wolfe Jr.*** of Baltimore, MD who proudly announces his marriage to Lisa C. Bauman on September 7 in Goshen, CT. Among those in attendance at the ceremony was ***Evan Weisman '92.*** Dr. Wolfe is currently working as a military physician with the rank of Captain at Aberdeen Proving Ground, MD.

'93

Gavin C. Barr of Springfield, NJ was named Chief Resident in the Emergency Medicine Program at New York University Medical Center. He will complete his training in June 1997.

Mary Ann G. Hanes of Havertown, PA and her husband, Dave Trephan, are the proud parents of Brian Alexander, born July 17, 1996.

Michael C. Sokol of Fort Lee, NJ completed his residency in Preventive Medicine at the University of Maryland Medical System in June. Michael now has an M.S. in addition to an M.D. after his name; he obtained a Master of Science degree in Epidemiology and Preventive Medicine while doing his residency. He is currently working for Merck-Medco Managed Care in Montvale, NJ as the Associate Director of Outcomes and Performance Assessment.

'96

David N. Ferraro Jr. of Pittsburgh, PA just had an addition to the family. Maria Elizabeth was born April 8, 1996 to David and Melanie.

A Green Thumb's Paradise

While many of us are facing snow, ***Edward Scull '48*** and his wife, Malelon, have escaped to warm Nevis in the West Indies. On this isle of emerald foliage, mountains, monkeys, and wild donkeys, Dr. Scull has cultivated his interest in horticulture. The Sculls first visited from Hartford, Connecticut (where he also gardened) in 1962, and a year later bought six acres including some old ruins. In 1982 Dr. Scull retired from his 30-year practice of rheumatology, and stayed on Nevis year-round.

He has raised more than 110 species of tropical fruit. Of his 500 orchids, many have been "naturalized" onto surrounding trees. "Every plant wants to grow," Dr. Scull theorizes. "If it dies, it's something I'm doing wrong."

—Malcolm Clendenin

"The Mill," a four-story structure dating from about 1800, houses living and sleeping areas amid the gardens.

Shop by Mail Orde

1 Olympic JMC T-Shirt S, M, L, XL	$14.95
2 Jacket: beige/blk, lined S, M, L, XL, XXL	$69.95
3 Baseball Cap: Wool/Suede	$14.95
4 Turtleneck: white, beige S, M, L, XL	$21.95
5 Basic Crew: gray, green, navy, burgundy	$29.95
Available Hooded: gray, green, navy, burgundy	$40.95
Available T-Shirt: gray, green, navy, burgundy	$14.95
6 Alumni Sweatshirt S, M, L, XL, XXL	$29.95
7 JMC Heavyweight Sweat	$57.95
8 JMC T-Shirt	$15.95
9 Jefferson Bottle Bag	$6.99
10 Golf Shirt Beige S, M, L, XL, XXL	$38.95
11 Knitted V-Neck Sweater S, M, L, XL, XXL	$59.95
12 Alumni T-Shirt: navy, gray, burgundy S, M, L, XL, XXL	$15.95
13 Caduceus T-Shirt: white, gray S, M, L, XL, XXL	$11.95

Kids' Corner

1 One Piece: Winged Ox 12M, 18M, 24M	$17.95
2 One Piece: Cow Jumped Over yellow or mint 6M, 12M, 18M, 24M	$16.95
3 One Piece: Short, Cow Jumped Over 6M, 12M, 18M, 24M	$12.95
4 Jump Suit: Winged Ox 12M, 18M, 24M	$16.95
5 Handpainted Bib "Rx 2 Hugs"	$5.95
6 Hooded Sweatshirt JMC 6M, 12M, 18M, 2T, 4T, 6, 8, 10, 12, 14	$24.95
7 JMC T-Shirt: gray, white 6M, 12M, 2T, 4T, 5	$10.95
8 JMC Baseball Cap: one size denim, orange, white	$8.95
9 Scrub Set: Bear Design 2T, 4T Bubble Gum Pink 2T, 4T, 5/6, 7/8, 10/12 Navy 2T, 4T, 5/6, 7/8, 10/12 Green 2T, 4T, 5/6, 7/8, 10/12	$14.95

Fax your order to JEFFERSON BOOKSTORE fax 215 923 1844

or mail to BOOKSTORE, 224 S. 11th Street, Philadelphia, PA 19107 (phone 215 955 7922)

Ship to: Name _____

Address _____

City _____ State _____ Zip _____

No cash or C.O.D. please. Orders must be prepaid.

ITEM	DESCRIPTION	COLOR	SIZE	QTY.	PRICE	TOTAL

Shipping and Handling: If your order totals $10.00 or less, add $3.00; $10.01 to $25.00, add $4.00; $25.01 or more, add $5.00. All items sent via U.P.S. Please allow 2–3 weeks for delivery.

MERCHANDISE TOTAL	
PA residents add 7% sales tax except on clothing	
SHIPPING AND HANDLING	
TOTAL	

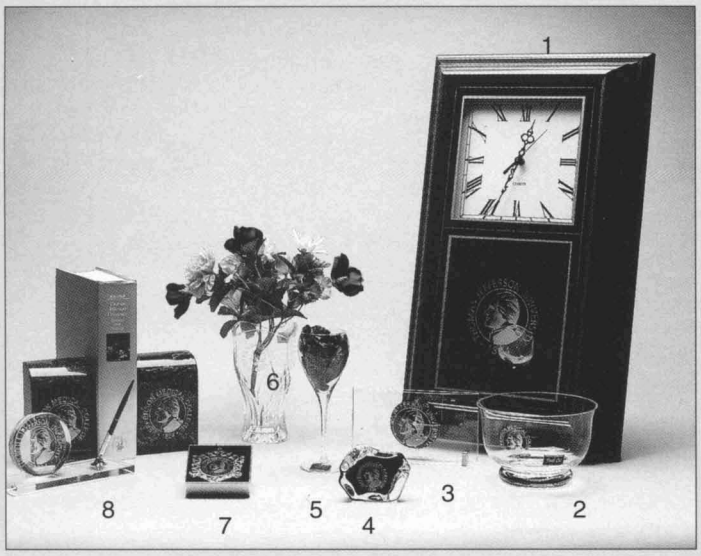
Method of Payment: ❑ Check (payable to TJU Bookstore) ❑ Visa ❑ MasterCard ❑ American Express ❑ Discover

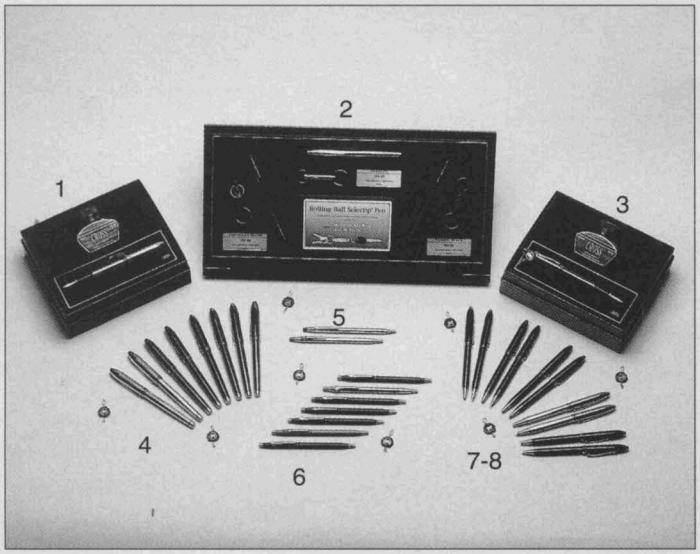
Account Number _____ Expiration Date _____

Signature _____ Date of Order ___/___/___ Daytime Phone _____

Return Policy: If you are not completely satisfied with the merchandise you have purchased, simply return the item with a copy of the packing slip and indicate the reason for the return. Your payment will be refunded within 30 days.

om the Jefferson Bookstore





Crystal Collection

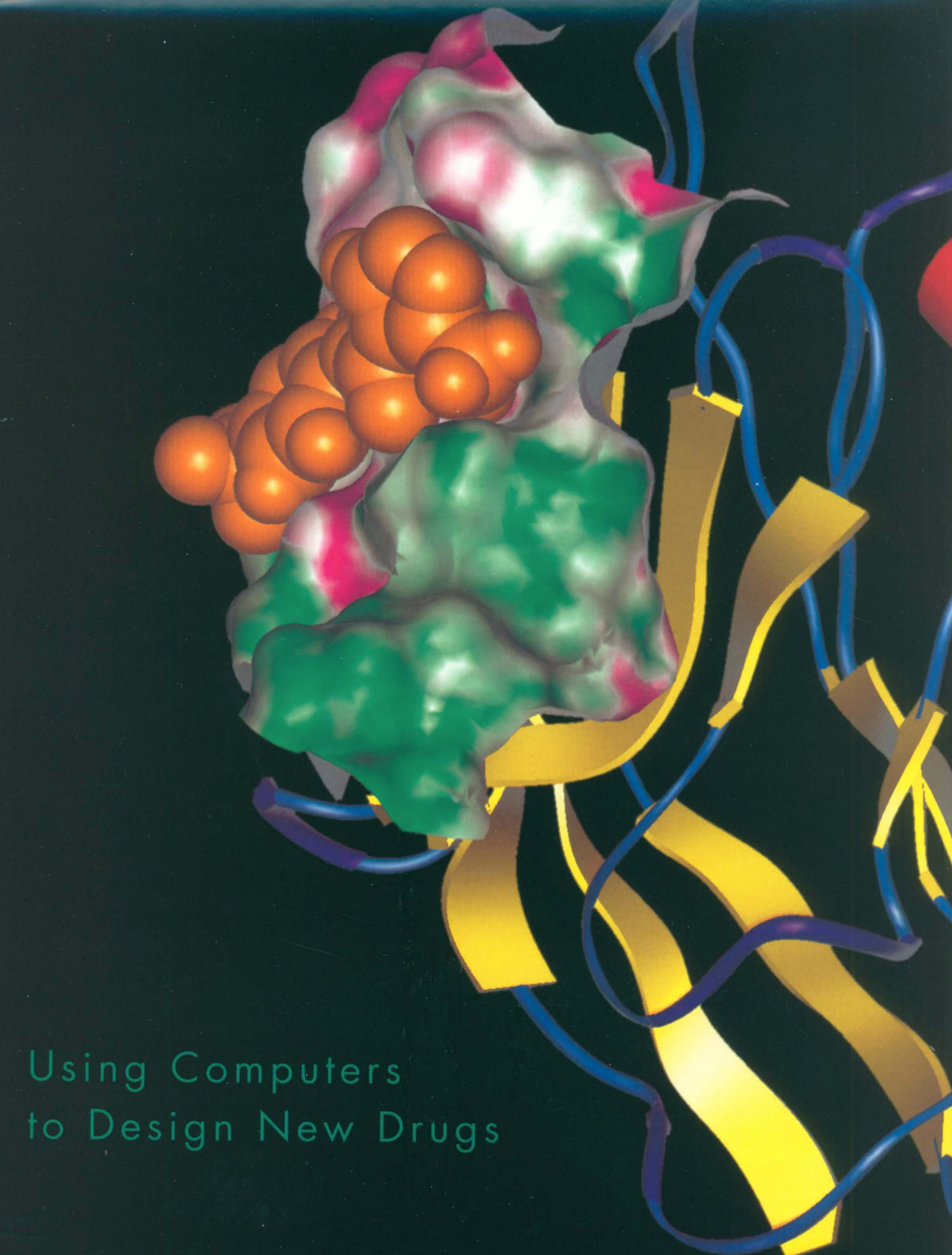
JMC engraved (personalized engraving available)	
1 Wall Clock: 15x26	$199.00
2 Revere Bowl	$74.95
3 Rectangular Clock	$79.00
4 Paperweight	$49.95
5 Wine Goblet	$24.00
6 Ancora Vase	$55.95
7 Snowflake Tree Ornament	$32.95
8 Desk Set (pen included)	$77.95
Marble Bookends	$89.95
Platter (not shown) 20x12	$79.90
TJU: Tradition and Heritage by Wagner	$120.00
TJU: Chronological History by Wagner and Savacool	$72.00
Gross Clinic Poster (not shown)	$19.95

Auto Mug 14oz	$4.99
Jefferson Canvas Lunch Bag	$7.99
Paper Cube: Winged Ox, Otter Fountain	$5.99
Pewter Glass Bottom Mug	$30.00
Stein: 32oz white/gold trim	$13.95
JMC Water Bottle	$3.99
JMC Citizen Watch: Men's	$119.95
JMC Citizen Watch: Ladies'	$119.95
Tie: Pediatric Doctor	$10.95
Tie: Anatomical	$29.95
a. DNA	
b. Eyeball	
c. Skeletal	
d. Heart	
Tie: Jefferson colors, Bl/Blk silk	$22.00
JMC Scarf: Faux Silk	$36.95
JMC Padfolio	$7.99
JMC Keychain	$4.99
JMC License Plate: Brass	$8.99
Silver	$7.99
Jefferson Postcards	$.50
Notecards: Winged Ox	$4.99
Pewter Letter Opener	$21.95
Duke Tankard: Pewter	$49.95

Cross Collection

1 Fountain Pen & Ink: Medalist	$85.95
2 Pen & Key Chain (Rollerball)	
Medalist	$39.95
Chrome	$31.95
Classic Black	$42.00
3 Fountain Pen & Ink: Titanium	$85.95
4 Rollerball Pens	$79.95
a. Black	
b. Sienna	
c. Green Marble	
d. Medalist	
e. Titanium	
5 JMC Chrome Set	$33.95
Available in Black	$50.95
6 JMC Ballpoint Pen:	$26.95
a. Black	
b. Navy	
c. Burgundy	
d. Grey	
Available in chrome	$17.95
7 Townsend Ballpoint Pen	$52.95
a. Sienna	
b. Black	
c. Green Marble	
d. Medalist	
e. Titanium	
8 Townsend Pencil	$51.95
a. Sienna	
b. Black	
c. Medalist	
d. Green Marble	
e. Titanium	

Ask for our catalog of multimedia software and medical supplies



Using Computers to Design New Drugs